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ABSTRACT

This report describes recent progress in knowledge on alcohol abuse and alcoholism. These topics are covered: (1) alcohol abuse and alcoholism, including drinking patterns, etiology, and alcohol dependence as a disease; (2) epidemiology, including morbidity and deaths; (3) genetics and environment, including twin and adoption studies, animal studies, potential markers of susceptibility, psychological and social processes, longitudinal studies generational trends in familial alcoholism, and perspectives on gene-environment; (4) neuroscience, including acute and chronic effects of alcohol, behavioral measures and alcohol as a reinforcing substance, and alcohol effects on the human brain; (5) medical consequences, including alcohol-induced liver disorders, effects on the gastrointestinal tract, nutritional and metabolic disorders, effects on the cardiovascular and immune systems, and effects on endocrine and reproductive functions; (6) fetal alcohol syndrome and other effects of alcohol on pregnancy outcomes, including clinical studies, research on the effects of prenatal alcohol exposure in animal models, studies on mechanisms of fetal alcohol damage, and public awareness and policy; (7) adverse social consequences, including accidents, suicide, trauma, crime and violence, and economic costs of alcohol abuse; (8) diagnosis and assessment of alcohol use disorders, including approaches to classifying alcohol use disorders and assessment; (9) prevention, including basic and applied research; (10) early and minimal intervention, including identification, intervening with drinking drivers, and employee assistance programs; (11) treatment, including management of alcohol dependence, components of treatment, and outcome evaluation methods. (ABL)

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Seventh Special Report
to the U.S. Congress on

ALCOHOL AND HEALTH

From the Secretary of
Health and Human Services
January 1990

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Alcohol, Drug Abuse, and Mental Health Administration
National Institute on Alcohol Abuse and Alcoholism

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Public Health Service
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National Institute on Alcohol Abuse and Alcoholism
5600 Fishers Lane
Rockville, Maryland 20857

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Foreword

Not more than 10 years ago, I was among the ranks of biomedical researchers seeking to understand how alcohol damages body systems. Understanding how something happens is, of course, the first step that must be taken before methods to prevent and treat the damage can be developed. As so evident in the *Seventh Special Report to the U.S. Congress on Alcohol and Health*, many of the first steps taken in alcoholism research over the years have resulted in important discoveries that have added significantly to our understanding of alcohol abuse and alcoholism and that will one day permit us to effectively prevent and treat one of our most pervasive public health problems.

The *Seventh Special Report to the U.S. Congress on Alcohol and Health* describes recent progress in our knowledge on alcohol abuse and alcoholism. Focused principally on research advances that have been made since the *Sixth Special Report* was issued in 1987, the report covers all active areas of research on alcohol-related problems including epidemiology, genetics, neurosciences, medical consequences of alcohol abuse and alcoholism, alcohol use and pregnancy, adverse social consequences of alcohol abuse and dependence, diagnostic criteria and screening instruments, prevention, intervention, and treatment. The report also provides a conceptual framework for alcohol-related research that, among other things, sets forth working definitions of alcohol abuse and alcoholism.

The *Seventh Special Report* clearly shows that steady progress continues to be made in all areas of alcohol-related research. Alcohol researchers in the basic sciences, such as the neurosciences, genetics, and molecular biology, have been able to use the very latest imaging technologies to make promising headway toward uncovering the biological antecedents for alcoholism. Because of our increasing ability to investigate the psychosocial or environmental factors involved in the development of alcohol-related problems, we are optimistic that the mix of environmental and genetic factors implicated in an individual's vulnerability to alcoholism can be identified. Doing so would provide health care professionals and others with a powerful tool for preventing alcohol abuse and alcoholism. Epidemiological research methodologies continue to be refined to permit more accurate pictures of how alcohol abuse and alcoholism impact on specific subsets of the general U.S. population. Progress also continues to be made in treating alcohol-related medical conditions. This is an area of continuing importance because it has been estimated that 20 to 40 percent of all U.S. hospital beds are occupied by persons whose health conditions are complications of alcohol abuse and alcoholism. Additionally, much progress has been made in developing and refining diagnostic and screening instruments to help clinicians identify and refer to treatment those of their patients with alcohol-related problems.

Since 1971, the Special Reports to Congress on Alcohol and Health have served as benchmarks of our progress toward eradicating the terrible impact of alcohol abuse and alcoholism on our Nation. Like its predecessors, the *Seventh Special Report* demonstrates that we have made many first steps and offers the promise of important steps yet to come.

Louis W. Sullivan, M.D.
Secretary
Health and Human Services

Preface

The United States Public Health Service, founded January 4, 1889, has just commemorated its 100th anniversary. Then, as now, preventing public health problems was a major focus of the Service, a focus that has been achieved for many diseases and disorders through continuing research on effective preventive techniques and public education to reduce risk for disease. The Special Reports to the U.S. Congress on Alcohol and Health describe current alcohol-related research findings that let us know that we are making progress and that help us to develop a vision for the future. However, these reports also serve another vital function—one that is very much within the traditions of the Public Health Service, that of providing current information on the health consequences of using alcoholic beverages. As such, the Special Reports on Alcohol and Health are an extremely effective vehicle to help educate the public about alcohol-related risks and to help individuals make informed lifestyle decisions to reduce or eliminate their risk for alcohol-related consequences.

There is no doubt that alcohol abuse and alcoholism are serious problems for the United States. An estimated 10.5 million U.S. adults exhibit some symptoms of alcoholism or alcohol dependence and an additional 7.2 million abuse alcohol, but do not yet show symptoms of dependence. Projections for 1995 suggest that 11.2 million will exhibit symptoms of alcohol dependence and the size of the group of alcohol abusers will not change. Alcohol use is associated with a wide variety of diseases and disorders, including liver disease, cancer, and cardiovascular problems. Although it is encouraging that deaths from liver cirrhosis, the principal cause of which is alcohol abuse, have been declining, cirrhosis of the liver caused almost 27,000 deaths and was the ninth leading cause of death in the United States in 1986.

Problems related to fetal exposure to alcohol also constitute a major public health problem; fetal exposure to alcohol is one of the leading known causes of mental retardation in the Western world and can be totally prevented. Accidental death, suicide, and homicide are significant causes of death, particularly for young men under age 34; nearly half of these violent deaths are alcohol related. More than 20,000 alcohol-related motor vehicle fatalities annually are attributed to alcohol abuse and these deaths are relatively more frequent among younger Americans. The costs of alcohol abuse to the Nation also are high. In 1986, alcohol abuse in the United States was estimated to cost $128.3 billion. Lost employment and reduced productivity accounted for more than half this amount. Health care for accidents and illnesses related to alcohol abuse, including alcoholism, liver cirrhosis, cancer, and diseases of the pancreas, was estimated to cost $16.5 billion.

Alcohol researchers are making significant and, in many cases, rapid progress toward developing methods to reduce the significant impact of alcohol abuse and alcoholism on our Nation. However, individual lifestyle choices will always have a major role to play in preventing disease and promoting health. For this reason, it is important for every citizen to read the information contained in the *Seventh Special Report to the U.S. Congress on Alcohol and Health*.

Today, we as a people are much more knowledgeable about our health needs than previous generations. It is my hope that Americans from all walks of life will find hope in the research progress found in the *Seventh Special Report to the U.S. Congress on Alcohol and Health* and information to help them achieve a healthier life.

James O. Mason, M.D., Dr.P.H.
Assistant Secretary for Health and
Acting Surgeon General

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This *Seventh Special Report to the U.S. Congress on Alcohol and Health* is the result of the cooperation of many people, whose combined efforts are reflected in the scientific accuracy and integrity of the document. The Editorial Review Board conceptualized the chapters, scientists recommended research articles, and both groups reviewed drafts of the chapters and suggested new research areas for inclusion. Science writers read and summarized thousands of articles to create the drafts and incorporated reviewers' changes to compose the final document.

This was truly a collaborative effort of scientists and science writers, guided by the Editorial Review Board. The chief contributors include some of the world's most distinguished alcohol researchers and medical authorities, many of whom also contributed to previous reports.

Contributors

Marlene Aldo-Benson, M.D.
Professor of Medicine, Immunology
and Microbiology
Rheumatology Division
Indiana University School of Medicine
Indianapolis, Indiana

Daniel J. Anderson, Ph.D.
President Emeritus
Hazelden Foundation
Center City, Minnesota

Thomas F. Babor, Ph.D.
Professor of Psychology
Department of Psychiatry
University of Connecticut
School of Medicine
Farmington, Connecticut

Raul Caetano, M.D., Ph.D.
Senior Scientist
Alcohol Research Group
Medical Research Institute of San Francisco
Berkeley, California

Theodore J. Cicero, Ph.D.
Professor of Neuropharmacology
Director, Neurobiology Laboratories
Department of Psychiatry
Washington University School of Medicine
St. Louis, Missouri

Sterling K. Clarren, M.D.
Aldrich Professor of Pediatrics
Division of Congenital Defects,
Embryology and Teratology
Department of Pediatrics
University of Washington
School of Medicine
Seattle, Washington

C. Robert Cloninger, M.D.
Professor and Head
Department of Psychiatry
Washington University School of Medicine
St. Louis, Missouri

Claire D. Coles, Ph.D.
Human and Behavior Genetics Laboratory
Assistant Professor
Department of Psychiatry
Emory University School of Medicine, and
Georgia Mental Health Institute
Atlanta, Georgia

John C. Crabbe, Jr., Ph.D.
Professor, Department of Medical Psychology
Associate Professor, Department
of Pharmacology
Oregon Health Sciences University, and
Research Career Scientist
Veterans Administration Medical Center
Portland, Oregon

Nancy L. Day, Ph.D.
Associate Professor of Psychiatry
and Epidemiology
Department of Psychiatry
Western Psychiatric Institute and Clinic
Pittsburgh, Pennsylvania

Ivan Diamond, M.D., Ph.D.
Director
Ernest Gallo Clinic and Research
Center, and
Professor and Vice-Chairman
Department of Neurology
University of California
San Francisco, California

Dennis Donovan, Ph.D.
Assistant Director
Addictions Treatment Center
Veterans Administration Medical Center, and
Associate Professor
Department of Psychiatry and
Behavioral Sciences
University of Washington School of Medicine
Seattle, Washington

Arthur Falek, Ph.D.
Professor of Psychiatry
Director
Laboratory of Human and Behavior Genetics
Georgia Addiction, Pregnancy, and
Parenting Project
Georgia Mental Health Institute, and
Emory University School of Medicine
Atlanta, Georgia

Kaye Fillmore, Ph.D.
Associate Professor
Institute for Health and Aging
University of California, San Francisco
San Francisco, California

Michael S. Goodstadt, Ph.D.
Director, Division of Prevention
Center of Alcohol Studies
Rutgers University
Piscataway, New Jersey

Michael Grossman, Ph.D.
Director, Health Economics
National Bureau of Economic Research, Inc., and
Distinguished Professor of Economics
City University of New York
New York, New York

Andrew C. Heath, D.Phil.
Associate Professor of Psychology
and Genetics in Psychiatry
Department of Psychiatry
Washington University School of Medicine
St. Louis, Missouri

Ralph Hingson, Sc.D.
Professor and Chief
Social and Behavioral Sciences
Boston University School of Public Health
Boston, Massachusetts

Barry Hoffer, M.D., Ph.D.
Professor
Department of Pharmacology
University of Colorado Health Sciences Center
Denver, Colorado

Theodore Jacob, Ph.D.
Professor of Family Studies
and of Psychology
Division of Family Studies
School of Family and Consumer Resources
University of Arizona
Tucson, Arizona

George F. Koob, Ph.D.
Associate Member
Department of Neuropharmacology
Research Institute of Scripps Clinic
La Jolla, California

Kenneth E. Leonard, Ph.D.
Senior Research Scientist
Research Institute on Alcoholism
New York State Division of
Alcoholism and Alcohol Abuse
Buffalo, New York

Ting-Kai Li, M.D.
Professor of Medicine and Biochemistry
Indiana University School of Medicine, and
Veterans Administration Medical Center
Indianapolis, Indiana

Charles S. Lieber, M.D.
Professor of Medicine and Pathology
Mount Sinai School of Medicine of the
City University of New York, and
Director, Alcohol Research and
Treatment Center and GI-Liver
Training Program
Veterans Administration Medical Center
Bronx, New York

Lawrence Lumeng, M.D.
Professor of Medicine and Biochemistry
Chief
Division of Gastroenterology and Hepatology
Indiana University, and
R.L. Roudebush Veterans Administration
Medical Centers
Indianapolis, Indiana

G. Alan Marlatt, Ph.D.
Professor
Department of Psychology
Director
Addictive Behaviors Research Center
University of Washington
Seattle, Washington

Roger Meyer, M.D.
Scientific Director
Alcohol Research Center, and
Professor and Chairman
Department of Psychiatry
University of Connecticut Medical School
Farmington, Connecticut

Klaus A. Miczek, Ph.D.
Professor
Department of Psychology
Tufts University
Medford, Massachusetts

William R. Miller, Ph.D.
Professor of Psychology and Psychiatry
Department of Psychology
University of New Mexico
Albuquerque, New Mexico

Robert M. Morse, M.D.
Director, Addictive Disorders
Professor of Psychiatry
Mayo Clinic
Rochester, Minnesota

Hector Orrego, M.D., F.R.C.P.(C)
Head, Gastroenterology Program
Addiction Research Foundation
Professor of Medicine and Pharmacology
University of Toronto
Toronto, Ontario, Canada

Oscar Parsons, Ph.D.
Executive Director
Center for Alcohol and Drug-Related Studies, and
Vice Head for Research
Department of Psychiatry and Behavioral Sciences
University of Oklahoma Health Sciences Center
Oklahoma City, Oklahoma

M.W. Bud Perrine, Ph.D.
Scientific Director
Vermont Alcohol Research Center
Burlington, Vermont

Theodore Reich, M.D.
Professor of Psychiatry & Genetics
Washington University School of Medicine
Psychiatrist in Chief
Department of Psychiatry
Jewish Hospital of St. Louis
St. Louis, Missouri

Robin Room, Ph.D.
Scientific Director
Alcohol Research Group
Medical Research Institute of San Francisco
Berkeley, California

Marcus A. Rothschild, M.D.
Chief, Nuclear Medicine Service
Veterans Administration Medical Center
New York, New York

Marcia Russell, Ph.D.
Research Scientist V
Research Institute on Alcoholism
Buffalo, New York

Herman H. Samson, Ph.D.
Director
Alcohol and Drug Abuse Institute
Professor
Department of Psychiatry and Behavioral Sciences
University of Washington
Seattle, Washington

Steven Schenker, M.D.
Professor of Medicine and Pharmacology
Chief
Division of Gastroenterology and Nutrition
The University of Texas
Health Science Center at San Antonio
San Antonio, Texas

Marc A. Schuckit, M.D.
Professor of Psychiatry
Alcoholism Research Center
Veterans Administration Hospital, and
University of California, San Diego
San Diego, California

Kenneth Sher, Ph.D.
Associate Professor
Department of Psychology
University of Missouri
Columbia, Missouri

Harvey A. Skinner, Ph.D.
Professor and Chairman
Department of Behavioral Science
University of Toronto, and
Senior Scientist
Addiction Research Foundation
Toronto, Ontario, Canada

Reginald Smart, Ph.D.
Director
Prevention Studies Department
Addiction Research Foundation
Toronto, Ontario, Canada

Robert J. Sokol, M.D.
Dean, School of Medicine
Professor
Department of Obstetrics and Gynecology
Wayne State University
Detroit, Michigan

Michael F. Sorrell, M.D.
Professor and Chairman
Department of Internal Medicine
University of Nebraska Medical Center
Omaha, Nebraska

Ralph Tarter, Ph.D.
Professor of Psychiatry and Neurology
Department of Psychiatry
Director
Center for Education and Drug Abuse Research
University of Pittsburgh School of Medicine
Pittsburgh, Pennsylvania

David H. Van Thiel, M.D.
Professor of Medicine,
Surgery and Psychiatry
University of Pittsburgh School of Medicine
Pittsburgh, Pennsylvania

Roger Dale Walker, Ph.D.
Professor
Department of Psychiatry
Chief, Addictions Research Center
Veterans Administration Hospital
University of Washington
Seattle, Washington

Diana Chapman Walsh, Ph.D.
Professor of Public Health and
University Professor
Boston University
Boston, Massachusetts

James R. West, Ph.D.
Professor
Department of Anatomy
College of Medicine
University of Iowa
Iowa City, Iowa

Harold L. Williams, Ph.D. (Deceased)
Distinguished Professor
Department of Psychiatry
Scientific Director
Oklahoma Center for Alcohol
and Drug-Related Studies
Oklahoma City, Oklahoma

Sharon C. Wilsnack, Ph.D.
Professor
Division of Psychiatry and Behavioral Science
Department of Neuroscience
University of North Dakota School of Medicine
Grand Forks, North Dakota

Editorial Review Board

CHAIR: Enoch Gordis, M.D.
Director
National Institute on Alcohol Abuse and Alcoholism
Rockville, Maryland

Rita L. Albery, R.N.
Project Officer, A&H VII
Office of Scientific Affairs
National Institute on Alcohol Abuse and Alcoholism
Rockville, Maryland

Loran D. Archer
Deputy Director
National Institute on Alcohol Abuse and Alcoholism
Rockville, Maryland

James D. Beard, Ph.D.
Director
Alcohol Research Center
Professor
Department of Psychiatry
University of Tennessee, Memphis, College of Medicine, and
Memphis Mental Health Institute
Memphis, Tennessee

Henri Begleiter, M.D., Ph.D.
Professor of Psychiatry and Neuroscience
SUNY Health Science Center at Brooklyn
Brooklyn, New York

Richard K. Fuller, M.D.
Director
Division of Clinical and Prevention Research
National Institute on Alcohol Abuse and Alcoholism
Rockville, Maryland

Donald Gallant, M.D.
Professor of Psychiatry and
Adjunct Professor of Pharmacology
Department of Psychiatry and Neurology
Tulane Medical Center
New Orleans, Louisiana

Thomas C. Harford, Ph.D.
Director
Division of Biometry and Epidemiology
National Institute on Alcohol Abuse and Alcoholism
Rockville, Maryland

Brenda G. Hewitt
Special Assistant to the Director
National Institute on Alcohol Abuse and Alcoholism
Rockville, Maryland

Harold D. Holder, Ph.D.
Director
Prevention Research Center
Berkeley, California

Yedy Israel, Ph.D.
Professor of Medicine
Department of Pharmacology
University of Toronto School of Medicine
Toronto, Ontario, Canada

Michael J. Lewis, Ph.D.
Visiting Scientist
Office of Scientific Affairs
National Institute on Alcohol Abuse and Alcoholism
Rockville, Maryland

W. Sue Shafer, Ph.D.
Acting Director
Division of Basic Research
National Institute on Alcohol Abuse and Alcoholism
Rockville, Maryland

Boris Tabakoff, Ph.D.
Director
Division of Intramural Clinical and Biological Research
National Institute on Alcohol Abuse and Alcoholism
Rockville, Maryland

Kenneth R. Warren, Ph.D.
Director
Office of Scientific Affairs
National Institute on Alcohol Abuse and Alcoholism
Rockville, Maryland

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Writers and Reviewers

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Introduction

In 1892 Franklin D. Clum, M.D., a physician who practiced in New York State, wrote the following words in his book entitled, *Inebriety: Its Causes, Its Results, Its Remedy*:

> Intemperance in the past has disgraced the palace and crown of the prince, the ermine of the judge, the sword of the chieftain, and the miter of the priest. Today it feasts alike upon the innocency of childhood, the beauty of youth, the amiableness of women, the talents of the great, and the experience of age.... The time has come for a study of inebriety from a medical stand-point, and when it is treated as a special disease its curability will be found equal to any other disease.

I do not believe that the book in which this statement appears is any longer in print; the copy from which this quotation was taken is from its third printing, and the book itself is now in a somewhat disheveled state. Yet the simple and eloquent conclusion reached by Dr. Clum, that alcoholism is a disease as worthy of serious study as any other disease, is as true today as it was 100 years ago. Nonetheless, today, as in the past, issues relating to what alcohol abuse and alcoholism are continue to cloud otherwise impressive gains made by the alcohol field toward finding effective ways to understand, prevent, and treat these continuing public health threats.

For many years, we in the alcohol field—researchers, clinicians, policymakers, recovering alcoholics, and other supporters alike—have fought hard to have alcohol-related problems recognized as major public health problems. To some extent, I believe we have been successful. Yet we find that there continues to be public uncertainty about whether alcoholism really is a disease, and if so, how it is distinguished from other forms of alcohol abuse. Although there may be many reasons for this, it is clear that part of the public's uncertainty stems from the differences that exist among experts on alcohol dependence over what to call these entities with which we deal, and attempts by nonexperts to fill the void with opinions that run counter to scientific fact as well as to the type of common sense demonstrated so ably by Dr. Clum.

The *Seventh Special Report to the U.S. Congress on Alcohol and Health* gives an accounting of how far we have progressed in our quest to unravel the mysteries of alcohol abuse and alcoholism since the publication of the last Special Report 3 years ago. It serves as a statement, based on current research findings, of what we know about the effects of alcohol abuse and alcoholism and their consequences on the individual, on groups, and on society. It also serves as a compendium of research hypotheses that are under investigation as we continue to broaden our understanding of the causes and potential solutions to abusive and dependent drinking. In these two respects, the *Seventh Special Report* is much like its predecessors. Unlike its forerunners, however, the *Seventh Special Report* provides, for the first time, a conceptual framework to clarify what is meant by the terms alcohol abuse and alcoholism.

This framework, as described in Chapter I of the *Seventh Special Report*, identifies three different types of drinkers. The first group is comprised of the majority of adult Americans who drink with few, if any, problems. The second group is made up of problem drinkers who are not dependent on alcohol but who develop difficulties secondary to alcohol consumption because of poor judgment, failure to understand the risks, or lack of concern about damage to themselves or others. This misuse of alcohol, in our conceptual framework, is termed alcohol abuse or nondependent problem drinking. Alcohol abusers are responsible for their behavior; they can often modify their alcohol consumption patterns in response to simple explanations and warnings and thus eliminate or reduce their risk for alcohol-related problems.

The third category of drinkers are individuals who are dependent on alcohol and who suffer from the disease called alcoholism or alcohol dependence. In the Chapter I conceptual framework, alcoholism or alcohol dependence is characterized as a disease with four main clinical features: (1) tolerance, or a state of adaptation in which more and more alcohol is needed to produce desired effects; (2) physical dependence, which means that upon interruption of drinking, a characteristic withdrawal syndrome appears that is relieved by more alcohol (e.g., morning drinking) or other drugs in the sedative group; (3) impaired control over regulating alcohol intake at any drinking occasion once drinking has begun; and, finally, (4) the discomfort of abstinence, or "craving," which can lead to relapse. In general, alcohol dependence can be viewed as a disorder of appetite; a pathological, or diseased, or abnormal appetite for a substance, alcohol, that is not present in individuals who are not alcohol dependent. Research findings described in the *Seventh Special Report* demonstrate that we are beginning to understand some of the scientific basis for alcohol dependence through biomedical research and research on environmental stressors that may be factors in an individual's susceptibility to and development of alcohol dependence. In the future, we will understand more and more about the nature of addiction, the portion of the vulnerability to addiction that is inherited, and the relationship between genetic and environmental factors leading to alcohol dependence in any one individual.

The issue of how to define alcohol abuse and alcoholism or alcohol dependence is a long-standing one and the conceptual framework for understanding the terms alcohol abuse and alcoholism discussed in the *Seventh Special Report* is by no means intended to be the last word. However, lack of concordance on definitions is not limited to the alcohol field. Although there is agreement on the major clinical features of major illnesses such as schizophrenia and rheumatoid arthritis, there is not yet complete agreement on the definition of these diseases. Yet, despite the lack of full agreement among specialists as to what these diseases are, progress continues to be made toward developing effective means to prevent and treat them. Similarly, the fact that there is not yet agreement in the alcohol field as to the precise definitions for alcohol abuse and alcohol dependence is not the important issue. Of greatest importance to our future as a field is the fact that there is agreement on the major clinical features for alcohol dependence, and it is this agreement that will make it possible for the alcohol field to progress despite the lack of commonly agreed upon definitions.

That our progress in alcoholism research continues to be steady and productive, I believe, cannot be seriously challenged; a comparison of research findings presented in the *First Special Report to the U.S. Congress on Alcohol and Health* with those in the *Seventh Special Report* will readily reveal this fact. Yet research does not happen in a vacuum; at the end of every test tube, mass spectrometer, nuclear magnetic imaging scanner, or sophisticated diagnostic instrument is one simple thing: the search for a way to eliminate the consequences of alcohol abuse and alcoholism. Conversely, only through a concerted research effort will currently available activities aimed at preventing and treating alcohol abuse and alcohol dependence be improved. This is the guiding principle in other major health areas, such as cancer, heart disease, and muscular dystrophy, and must become the guiding principle in the alcohol field as well.

Alcohol-related research can provide the answers, in time, as to what alcohol abuse and alcohol dependence are and how to successfully prevent and treat them. However, I believe that it is only through our collective struggle as a field to reach this goal that we will ultimately succeed.

Enoch Gordis, M.D.
Director
National Institute on Alcohol Abuse
and Alcoholism

Alcohol and Health—An Overview

Section 506(a) of the Public Health Service Act requires that the Secretary of Health and Human Services submit to the U.S. Congress a report that contains current information on the health consequences of using alcoholic beverages and a description of current research findings on alcohol abuse and alcoholism. The *Seventh Special Report to the U.S. Congress on Alcohol and Health*, prepared in accordance with that requirement, focuses on research advances since publication of the *Sixth Special Report* in January 1987. Major highlights of the report are presented in the following sections.

CHAPTER I: Alcohol Abuse and Alcoholism

Alcohol abuse and dependence (i.e., alcoholism) are serious problems that affect about 10 percent of adult Americans. Adverse social and medical consequences of abusive drinking arise from single bouts of drinking, as well as from longer term effects of alcohol consumption. Adverse consequences may affect not only the drinker, but also others with whom the drinker comes in contact. A minimum of 3 out of 100 deaths in the United States can be attributed to alcohol-related causes.

Two distinct forms of problematic drinking—alcohol abuse and alcohol dependence—have been identified. Alcohol abuse involves patterns of heavy alcohol intake in nondependent persons in which health consequences and/or impairment in social functioning are associated. Alcohol dependence is differentiated from alcohol abuse on the basis of such manifestations as craving, tolerance, and physical dependence that result in changes in the importance of drinking in one's life and in impairment of the ability to exercise restraint over drinking.

Both alcohol abuse and dependence arise as a result of different, complex, and as yet incompletely understood processes. Evidence for genetic transmission of vulnerability for alcoholism has been provided by twin and adoption studies. The mechanisms of genetic transmission are unknown, however, as are the specific environmental factors that interact with genetic predisposition in the development of alcoholism. Research has shown that psychological and social factors and factors in the home environment influence an individual's drinking behavior. Genetic predisposition does not imply predestination, however, and research aimed at the identification of factors associated with resistance is of interest.

Alcohol research has provided the foundation of knowledge on which an understanding of key issues regarding the causes, prevention, and treatment of alcohol abuse and alcoholism is built. Still, much is to be learned and many questions are yet to be answered. A particularly rich source of new knowledge and potentially important advances in understanding is future research on alcohol abuse and alcohol dependence that draws from both biological and behavioral sciences. In science, boundary areas between disciplines represent unique opportunities for cooperation and exciting prospects for advancement.

CHAPTER II: Epidemiology

In 1987, after 6 successive years of gradual but consistent decline, per capita consumption of alcohol in the United States was at its lowest level since 1970. Nevertheless, alcohol is used by more Americans than any other drug, including cigarette tobacco. In terms of consumption patterns, population surveys indicate increases in abstention, especially among men, and decreases in alcohol consumption among adolescents. Yet, there is evidence of an increase in the proportion of heavy drinkers among both men and women in their twenties and of a small increase in the prevalence of dependence symptoms—findings which underline the importance of continued surveillance.

Alcohol epidemiologic research includes studies of population subsets. Gender-specific differences in drinking patterns and problems have been found, and research examining factors associated with women's drinking has been conducted, including research on the relationship between alcohol-related problems and various roles assumed by women. Differences in alcohol use patterns and vulnerability to alcohol-related problems among major racial and ethnic groups in the United States have also been found. Alcohol abuse and dependence are serious problems for the homeless, among whom prevalence estimates for current alcohol-related difficulties range from 20 to 45 percent.

Age-related differences in drinking patterns and problems have also been identified. Both heavy drinking and drinking-related problems are associated with being male, young, and/or unmarried; however, there is a high degree of remission of problems with increasing age which parallel age-related decreases in heavy drinking. The gradual downward trend in alcohol use by high school seniors during the 1980s continued through 1988. Yet, alcohol use was still disturbingly high: 92 percent of seniors in 1988 had tried alcohol, nearly two-thirds were current drinkers, and more than one-third were occasional heavy drinkers.

The prevalence of alcohol-related problems among hospitalized persons has been estimated to be 25 percent. Comorbidity of alcohol-related diagnoses with other disorders has been found to include disorders of the liver, pancreas, digestive tract, respiratory system, nervous system, and cardiovascular system, as well as drug abuse, mental illness, injuries and accidents, infections, anemias, and malnutrition.

CHAPTER III: Genetics and Environment

The observation that alcoholism tends to run in families has been confirmed by numerous reports in the scientific literature. Traits that are familial may be passed from generation to generation by genetic factors or by environmental factors. In alcoholism, the interaction of genetic and environmental factors is emerging as a fundamentally important research issue.

Although the mechanisms of genetic transmission are not yet known, evidence for genetic transmission of vulnerability for alcoholism has been provided by twin and adoption studies. Genetic involvement is also suggested by studies of animal lines selectively bred to differ in a number of alcohol-relevant traits, and by studies of potential biological markers of susceptibility.

Such psychological and social factors as cultural and group norms, peer influences, expectancies about alcohol's effects, and subjective experiences of alcohol's pharmacologic effects have been found to influence drinking behavior. Problems in the childhood home and childhood behavioral difficulties have been observed as antecedents of alcohol dependence, but a causal role has not been established. There is considerable research interest in expectancies, including the effect on drinking behavior of expectations about alcohol's specific actions and about alcohol's effects on coping and social functioning.

Some forms of alcohol dependence are highly heritable, while others are less so; there are also instances of alcoholism without obvious genetic involvement. Thus, many persons having family histories indicative of risk do not develop alcohol dependence since it is the interaction of genetic and environmental factors that define vulnerability. That is, even if facilitative genes are inherited, they may not be expressed in the absence of provocative environmental factors.

The systematic study of gene-environment interactions in the etiology of alcoholism has barely begun. It is encouraging, however, that researchers in the field are beginning to draw on knowledge from both the biological and psychosocial literature on alcohol-related behaviors to formulate gene-environment hypotheses that can be tested. In the future, there will be great opportunities for cooperation among scientists representing biological, psychological, and social perspectives and exciting prospects for advances in our understanding of the causes of alcoholism.

CHAPTER IV: Neuroscience

Neuroscience research on alcohol abuse and dependence is progressing rapidly with investigations attempting to uncover the molecular, cellular, and behavioral bases for alcohol's actions on the brain. In particular, there is sufficient evidence that doses of alcohol which typify common consumption affect specific proteins along brain cell membranes; in contrast, previous research suggested that alcohol affects the brain primarily by altering the membrane lipid bilayer.

The proteins that have been of interest to alcohol researchers are involved in the function of a number of neurotransmitters such as GABA, glycine, and glutamate. Research on one glutamate receptor has been especially encouraging because a number of activities regulated or controlled at this receptor, including memory, seizure threshold, and cell growth during fetal development, are known to be altered by alcohol consumption. Other proteins that have been of interest to alcohol researchers are those that control the opening and closing of ion channels; recent studies have demonstrated how chloride and calcium channels in particular are affected by alcohol use.

In addition, studies have demonstrated that both acute and chronic administration of alcohol alters the activities of "second messenger systems." Second messenger activities are fundamental to cellular well-being. The effects of alcohol on one second messenger system, the adenylate cyclase complex, have received much attention because it has been found that one of this system's subunits, the G protein subunit, is especially vulnerable to alcohol.

Chronic alcohol use can lead to the states of tolerance and dependence. Alcohol researchers have found that certain neurohormones such as vasopressin may play a critical role in maintaining tolerance and that other neurotransmitters, receptors, and ions such as calcium may play a role in mediating tolerance to alcohol. Chronic exposure to alcohol also alters properties of membrane lipid bilayers in the brain as well as in other tissues that may significantly change a host of lipid and protein-regulated functions.

Studies investigating the effects of alcohol on the human brain have been made possible by new, noninvasive techniques for recording brain wave activity. Studies have shown that sons of alcoholics display some unique electrophysiological behaviors. These studies are intriguing because they suggest that alterations in the brain's electrical activity serve as biological markers for predisposition to alcoholism.

CHAPTER V: Medical Consequences

Alcohol affects almost every organ system in the body either directly or indirectly. The liver (the primary site of alcohol metabolism) is susceptible to injury of three major types: fatty liver and alcoholic hepatitis, which may be reversible with abstinence, and cirrhosis, which is irreversible. The encouraging news is that mortality from cirrhosis has been declining steadily since 1973 for reasons that are not yet clear. Nevertheless, cirrhosis mortality was the ninth leading cause of death in the United States in 1986.

Liver transplantation is a therapeutic modality that has been used successfully for advanced or end stage alcoholic liver disease. In a major ongoing study of liver transplantation, the 1-year survival rate of 73 percent and the 2-year survival of 64 percent in patients with alcoholic liver disease did not differ from survival rates for nonalcoholic controls. Further, recidivism to alcoholism has been quite low.

In the gastrointestinal tract, regular alcohol use can precipitate esophagitis and exacerbate existing peptic ulcers. The relative risk of esophageal cancer is higher among alcohol abusers, as is the incidence of chronic gastric carcinoma. Heavy alcohol consumption is also a principal cause of chronic pancreatitis.

Alcohol accounts for more than 10 percent of the total caloric intake of some adult drinkers in the United States, and nutritional deficiencies, including anemia, neuropathy, and Wernicke's disease, are a frequent complication of alcohol dependence. In addition, alcohol has been found to have profound metabolic effects on carbohydrate, lipid, and protein metabolism. Chronic alcohol abusers can develop clinical signs of cardiac dysfunction, and up to 50 percent of excess mortality in alcoholics and heavy drinkers can be attributed to cardiovascular disorders. Furthermore, chronic alcohol consumption is associated with a significant increase in hypertension.

Alcohol affects immune, endocrine, and reproductive functions. Heavy alcohol consumption is also a well-documented cause of neurological problems, including dementia, blackouts, seizures, hallucinations, and peripheral neuropathy.

New concepts and recent technological advances have great potential to accelerate progress in understanding the biomedical consequences of alcoholism and in developing improved methods to treat and prevent the consequences of alcohol abuse and dependence.

CHAPTER VI: Fetal Alcohol Syndrome

Problems related to fetal exposure to alcohol constitute a major public health problem: Fetal exposure to alcohol is one of the leading known causes of mental retardation in the Western world. Moreover, treatment costs associated with such exposure are estimated at nearly one-third of a billion dollars annually.

The deleterious consequences of maternal drinking during pregnancy are long lasting. Although a followup study of fetal alcohol syndrome cases in Germany showed improvement over time on several parameters, particularly with regard to physical appearance, cognitive deficiencies persisted.

Not all women who drink alcohol excessively during pregnancy deliver babies with fetal alcohol syndrome or fetal alcohol effects. Genetic and maternal variables may account for differences in outcome and may explain why some infants are spared. Epidemiologic research has shown that black infants are more susceptible, but the ubiquity of the disorder throughout the world indicates that no group is immune.

Animal research has played a major role in advancing our knowledge of the detrimental consequences that follow prenatal alcohol exposure. For example, animal studies suggest that peak blood alcohol concentration levels, rather than amount consumed per se, represent a critical factor.

Research suggests that a number of biological and behavioral factors may be useful in identifying women at greater risk for continued alcohol abuse during pregnancy. Research has shown that the best predictors of continued drinking during pregnancy were length of drinking history, reported tolerance to alcohol, and history of alcohol-related illness. The importance of identifying and targeting high-risk women for intensive prevention efforts is best underscored by the research findings of significant compromises in pregnancy outcome in women who continued to drink throughout pregnancy compared with women who abstained or stopped drinking at some point during pregnancy.

When surveyed concerning their health awareness, 84 percent associated the risk for adverse pregnancy outcomes with heavy drinking, but among the 55 percent who had heard of fetal alcohol syndrome, only one in four correctly identified it as a set of birth defects. This is indicative of the need for increased public awareness about fetal alcohol syndrome.

CHAPTER VII: Adverse Social Consequences

Adverse social consequences arise as a result of single episodes of drinking, persistent alcohol abuse, and alcohol dependence. Alcohol consumption can result in consequences ranging from problems with one's family, friends, employers, and the police to alcohol-related injuries, illnesses, and death.

Alcohol has been implicated in the leading causes of accidental death in the United States—motor vehicle crashes, falls, and fires and burns. Of these, motor vehicle crashes are the leading cause of injury deaths. Although the proportion of all people killed in crashes in which at least one participant was legally intoxicated declined from 46 percent in 1982 to 40 percent in 1987, traffic crashes remain the greatest single cause of death in the United States for people between the ages of 5 and 34. It has been estimated that the risk of a fatal crash, per mile driven, is at least eight times higher for a drunk driver than for a sober one, and approximately one-half of all crash fatalities are alcohol related.

Although less is known about alcohol involvement in other types of accidents, research findings suggest that alcohol increases the risk for falls, fires, and burns. Research also indicates that 20 to 36 percent of suicide victims have a history of alcohol abuse or were drinking shortly before their suicides, and that alcohol tends to be associated with suicides that are impulsive rather than premeditated.

The extent of injuries sustained in alcohol-involved accidents, suicides, and suicide attempts may be influenced by the victim's drinking history or recent alcohol consumption. Intoxication is frequently found among trauma victims: A survey of emergency room trauma cases, for example, found that 20 to 37 percent of all such cases involved alcohol. Further, intoxication negatively influences the outcome for motorcyclists who are trauma victims and for pedestrians who are injured in motor vehicle accidents.

The economic cost of alcohol abuse and dependence is high. For example, untreated alcoholics and their families have higher general health care costs than nonalcoholics and their families, but the pattern of health care costs for alcoholism has been found to be similar to other chronic diseases, including hypertension and diabetes. General health care costs tend to decrease following alcoholism treatment.

CHAPTER VIII: Diagnosis and Assessment of Alcohol Use Disorders

Diagnostic criteria in the current revised version of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III-R) and the World Health Organization's *International Classification of Diseases* (ICD-9) employ definitions that differentiate a nondependent problem drinking condition (alcohol abuse) from alcohol dependence (alcoholism). Alcohol abuse represents a pattern of heavy drinking accompanied by social, psychological, and/or medical problems that are directly related to alcohol use, while alcoholism is characterized by physical and psychological dependence that results in impaired control over drinking. Both diagnostic systems offer specific criteria to guide the diagnostic process and represent a general evolution toward detailed assessment of alcohol use disorders using multiple criteria.

Screening is an important preliminary step in the diagnosis of alcohol use disorders that is needed to ensure early identification of individuals who have begun to develop or who are at risk for developing alcohol use problems. Screening tests serve to direct persons toward further assessment. Assessment provides more detailed information about the individual's alcohol problems and is used in planning intervention and treatment.

Research has explored the reliability and validity of self-report procedures, such as questionnaires that assess psychological and social indicators of alcohol difficulties, and improved methods, including computerized assessment, have been examined. Several screening instruments have been found particularly useful in identifying alcoholics. Laboratory tests are frequently used to corroborate the results of other assessments, and biochemical tests are valuable for hospital-based physicians in detecting hidden alcohol use disorders. The sensitivity and specificity of such tests has also been the subject of research. Because each type of assessment method has some limitations, methods that combine self-report, clinical examination, and laboratory tests have been designed.

Although primary care physicians are in a key position to make early diagnoses of alcohol use disorders, they may misdiagnose or underdiagnose because of stereotypes regarding alcohol problems or inadequate training in this area. The coexistence of alcohol use disorders and psychiatric disorders also can complicate the diagnostic process.

CHAPTER IX: Prevention

Prevention activities are directed at drinkers in general, at problem drinkers, and at those at risk for the development of problematic drinking. Prevention strategies attempt to avert the adverse effects of single bouts of drinking and to mitigate the effects of long-term abusive drinking.

Research investigating the relationship between the price of alcoholic beverages and alcohol use problems such as motor vehicle crashes continues to be one of the most promising research areas related to prevention. Evidence suggesting that alcohol tax increases are associated with decreases in the amount of alcohol consumed, fatal traffic crashes among youthful drivers, and mortality rates for liver cirrhosis has been provided.

The increase in the minimum drinking age from 18 to 21 has also been demonstrated to be an effective prevention strategy. Research on the effect of the minimum drinking age found that the greatest reduction in fatal traffic accidents involving drinking drivers was among 16- to 20-year-olds in States that increased their minimum drinking age to 21.

Although evaluations of programs aimed at deterrence of drinking and driving in individual States have varied in their conclusions, a recent national study found that "per se" laws that define driving while intoxicated (DWI) using blood alcohol concentration thresholds, administrative suspension or revocation laws, and laws that mandate jail or community service for

DWI first offenders each played a role in the decline of fatal alcohol-involved crashes.

Data on server training programs, a relatively new approach to reducing the incidence of drunk driving, are becoming available. Evaluations of these programs, though few in number, suggest that server training may have a positive effect in increasing server efforts to reduce the rate and amount of alcohol served and decreasing the amount consumed by patrons.

Recent research has studied prevention efforts focused on school-age children that employ a cognitive-behavioral approach and often involve interventions intended to improve general coping skills. Although results have been mixed, there is some evidence of short-term effects and of reductions in the amount of drinking among young people. Other prevention approaches, such as those emphasizing alcohol education, have been found to increase young people's knowledge about alcohol and its effects, but generally have not been successful in changing attitudes or behavior.

CHAPTER X: Early and Minimal Intervention

Early intervention targets individuals who are at risk for developing alcohol-related problems or who are experiencing adverse effects of drinking but who are not alcohol dependent. The intervention process includes both identifying such individuals and modifying their drinking patterns and their drinking-related behaviors and attitudes.

Elements of early and minimal interventions include combinations of brief advice and assessment interventions, feedback and admonition sessions, and self-help behavioral training manuals. Because minimal approaches to early intervention emphasize self-management techniques, there is little cost or professional involvement. Research is not extensive, but some investigations in the United States, New Zealand, Scotland, and Sweden suggest that relatively simple approaches to intervention can affect drinking patterns and alcohol-related problems.

Controlled drinking is not an appropriate treatment goal for alcoholics, but alcohol abusers (i.e., individuals who are not dependent) may benefit from interventions aimed at moderating their alcohol consumption. Behavioral self control training is the most frequently used approach. Research concerning its effectiveness is limited and has thus far produced mixed results.

The arrest of drinking drivers can result in early identification of alcohol problems and provides an opportunity for intervention. The need to consider the characteristics of individual DWI offenders as a means of improving the effectiveness of interventions for this population has been emphasized. Findings of recent research suggest that interventions for drivers at risk for DWI offenses should address their general propensity to engage in risky behavior, heavy alcohol consumption, and skills at estimating blood alcohol concentration.

The growth of employee assistance programs (EAPs), which help workers with alcohol use problems, has continued. However, systematic research evaluating the effectiveness of such programs remains limited.

CHAPTER XI: Treatment

Alcohol dependence (alcoholism) is a serious disease that affects the health and well-being of millions of Americans. More than 1.43 million people were treated for alcoholism in fiscal year 1987, the majority in outpatient settings. The components of treatment include management of alcohol withdrawal, long-term management of alcohol dependence, and prevention of relapse.

For alcohol-dependent persons, the appropriate treatment goal is abstinence. To this end, a range of treatment options is available, including pharmacologic interventions, psychotherapy and counseling, Alcoholics Anonymous (AA), and a variety of behavioral training programs. Research on the effectiveness of various treatment approaches has improved knowledge about the effectiveness of group therapy, spousal involvement in alcoholism treatment, marital therapies, social skills training, and AA. The effectiveness of various pharmacologic agents has been investigated, including drugs that are used in the medical management of alcohol withdrawal syndrome and drugs that foster sobriety by interfering with the metabolism of alcohol, thereby producing a noxious reaction when alcohol is ingested.

Alcohol-dependent persons do not represent a homogeneous group. Important aspects of heterogeneity among alcoholics include highly varied psychiatric comorbidity, differences in personality, life experiences, family background, and social status. Two clinical subtypes of alcoholism based on genetic studies have also been identified. Knowledge of the differences among alcohol-dependent persons is important because research has shown that alcoholism treatment methods are differentially effective based on patient characteristics.

This has led to considerable interest in patient treatment matching. Differences in social functioning and in psychopathology have been investigated in terms of specific treatment approaches, and variations in intensity, structure, and type of treatment have been explored in relation to patient characteristics. Although important findings about patient treatment matching for individual studies have been reported, it remains for large-scale trials to develop findings that are generalizable.

Conclusion

This report contains much new information on the health consequences of using alcoholic beverages and presents current research findings on alcohol abuse and alcoholism. Significant research advances have taken place since the publication of the *Sixth Special Report* in January 1987, yet there are many areas in which research must continue.

■ Chapter I

Alcohol Abuse and Alcoholism

Introduction

Alcohol research has provided the foundation of knowledge on which an understanding of key issues regarding the causes, treatment, and prevention of alcohol abuse and alcoholism can be built. Because alcohol consumption is clearly not a risk-free activity, the central question of alcohol research is why some people continue, despite compelling evidence of harm, to consume large quantities of a substance that engenders a host of adverse physical, psychological, and social consequences. More specifically, alcohol research is aimed at determining the reasons that people drink, the reasons they continue to drink even though alcohol use creates problems for them, and the reasons that some are unable to stop drinking even in the face of highly detrimental outcomes.

Adverse consequences can arise both from single bouts of drinking as well as from long-term social and medical effects, and the toll is high: A minimum of 3 out of 100 deaths in the United States can be attributed to causes linked directly to alcohol (Van Natta et al. 1984–85). In addition to traffic crashes, alcohol-involved injuries and deaths, serious medical consequences, and birth defects, alcohol abuse has been implicated in aggression, crime, marital discord, and job loss. Alcohol-related consequences can affect not only drinkers themselves, but also their spouses, children, friends, and employers, as well as strangers with whom they may come in contact. Further, serious economic consequences have been observed: The cost of alcohol abuse and alcohol dependence was estimated at $116.9 billion in 1983, of which 61 percent was attributed to lost employment and reduced productivity and 13 percent to health care costs (Harwood et al. 1985).

This chapter provides an overview of issues related to alcohol research. In particular, historical, diagnostic, clinical, and etiological matters related to patterns of problematic drinking, alcohol abuse, and alcohol dependence (alcoholism) are discussed.

Drinking Patterns

Drinkers display many different patterns of alcohol use. The majority of drinkers are those for whom drinking produces no serious long-term health or social consequences and cessation of alcohol use poses no problem. These persons are referred to as social drinkers. Though these individuals do not experience the effects of chronic alcohol abuse, they *are* nonetheless at risk for adverse consequences arising from single bouts of drinking such as alcohol-related accidents. Persons who experience a variety of social and medical problems as a result of high-risk drinking but who are not dependent on alcohol are called alcohol abusers or nondependent problem drinkers. Alcohol use by these individuals often leads to problems that arise from impaired judgment, diminished concern about the consequences of behavior, and physical effects of alcohol consumption. Such adverse events may be the result of a single bout of drinking, or they may represent the effects of persistent high-risk alcohol use.

Finally, there are alcoholics—or alcohol-dependent persons. Not only do alcoholics experience adverse consequences from single bouts of drinking and social and medical consequences from chronic high-risk alcohol use, but they also experience physical and psychological dependence on alcohol that results in impaired ability to control drinking behavior. This impairment in control represents the critical distinction between alcohol abuse and alcohol dependence.

Not all drinkers, however, fit neatly into one category or another and degrees of severity of both alcohol abuse and alcohol dependence have been identified. Periodic high-risk drinking by individuals generally thought to be social drinkers can cause serious problems such as alcohol-involved injuries, yet these individuals may not satisfy the clinical criteria that define alcohol abuse. Similarly, persistent and repetitive alcohol abuse that causes severe social and medical problems may be difficult to differentiate from alcohol dependence. The risk for acute alcohol-involved problems varies from setting to setting, so that alcohol use that would create minimal difficulties in one situation may prove deadly in another (e.g., drinking at home then going to bed versus drinking at a tavern then driving home).

In terms of prevalence, a household survey of persons aged 18 and older found that 34 percent of respondents were nondrinkers; 56 percent were nondependent, nonproblem drinkers (analogous to social drinkers as described in the preceding paragraphs); 4 percent, nondependent problem drinkers (i.e., alcohol abusers); and 6 percent, alcohol dependent (Harford and Parker 1985). In the Epidemiological Catchment Area studies that sampled both household and institutional populations in an investigation of the prevalence of psychiatric disorders in three cities, alcohol abuse and alcohol dependence were combined into a single category. In these studies, lifetime prevalence rates of alcohol abuse and dependence (the proportion of the population that had ever experienced the disorder) of 11.5 percent, 13.7 percent, and 15.7 percent, respectively, were found (Robins et al. 1984).

Examinations of the differences and similarities between patterns of alcohol use have revealed no unvarying or inevitable sequence of behaviors and symptoms leading from one drinking classification to another. Thus, an individual drinker can display more than one drinking pattern during his or her lifetime, and although many people may drink alcoholic beverages and experience few or no adverse effects from their drinking, some drinkers become alcohol abusers or alcohol dependent. For certain individuals, drinking is problematic from the start. For an unfortunate few, a single exposure to alcohol can herald the onset of addiction, but, for most, alcohol dependence takes a few years to develop. Not all of those who abuse alcohol go on to become dependent, and some ferry back and forth between periods of nonproblem drinking and periods when alcohol use is problematic. Further, just as an individual can be an alcohol abuser without being dependent, individuals can be alcohol dependent before they manifest alcohol-related social and medical problems.

Although there is evidence for progression of alcohol dependence symptoms that describes the developmental sequence once a person becomes dependent (Mandell 1983), no consistent picture characterizing this progression has emerged. Jellinek (1952) proposed that alcoholism is characterized by symptom progression through three phases; Trice and Wahl (1958) suggested that alcoholism involves movement from one symptom cluster to another as opposed to movement from one symptom to the next; Orford and Hawker (1974) suggested that three predictable symptom clusters occur sequentially but noted that many other phenomena occur in random fashion as alcoholism develops. More recently, Piazza and Wise (1988) also investigated developmental progression. Although the sequence they described is consistent with Jellinek's observation that impaired control marks the onset of alcoholism, it otherwise differed substantially from that proposed by Jellinek.

The development of problematic use of alcohol involves factors associated with initiation of use, the transition to abuse or dependence, and overcoming abuse or dependence (Marlatt et al. 1988). These factors have provided a useful framework for alcohol research, including research involving biological and psychosocial influences on drinking behavior. The research field, however, is only beginning to apply definitions that clearly and consistently differentiate between alcohol abuse and alcohol dependence. As research in this area continues, understanding of the development and progression of alcohol abuse and alcohol dependence will be improved.

Historical Perspective

In 1784 in "An Inquiry into the Effects of Ardent Spirits upon the Human Body and Mind," Benjamin Rush, a physician and signer of the Declaration of Independence, described drunkenness as a disease, listed its acute and chronic manifestations, and observed hereditary and nongenetic influences in its occurrence. Historically, the explanation of alcoholism as a disease stood in contrast to moral explanations in which character defects were believed to lead to sinful drinking behavior that the individual had to conquer by dint of will (Marlatt et al. 1988). Jellinek (1960) reported that scientific examination of alcoholism beginning in the 1930s was based on the understanding of alcoholism as a disease, but that hypotheses about the nature of the disease—i.e., psychological, allergic, nutritional, biochemical, endocrinological, or neurological—varied widely. Although Jellinek (1960) proposed typologies, he defined alcoholism broadly as any drinking having harmful consequences.

Clinical Differentiation of Alcohol Abuse and Alcohol Dependence

As evidence mounted suggesting that alcoholism represents the interaction of environmental factors with specific biological mechanisms manifested in behavior, it became clear that two distinct forms of problematic drinking exist—alcohol abuse and alcohol dependence. The work of Edwards and his colleagues (Edwards et al. 1977; Edwards and Gross 1976) has been aimed at identifying the two forms and distinguishing between them. Drinking problems occur either as "alcohol-related disabilities" or "alcohol dependence syndrome"; the former term describes problems in accomplishing basic living activities in which alcohol is implicated that may be transitory or long term; the latter term describes a severe disability in which dependence brings about a reduction in the individual's ability to control the drinking behavior (Edwards et al. 1977). A similar delineation was recently employed by the Institute of Medicine (IOM 1987, p. 17), which defined alcohol abuse as "a heterogeneous set of behaviors characterized by repetitive patterns of heavy drinking associated with impairment of psychologic or social functioning and/or health" and discussed alcoholism as a separate entity. Difficulties in framing a definition of alcohol dependence have been noted (IOM 1987; Caetano 1987), but alcohol dependence is consistently differentiated from alcohol abuse on the basis of development of such manifestations as craving, tolerance, and physical dependence that bring about changes in the importance of drinking in one's life and in impairment in the ability to exercise behavioral restraint (Edwards et al. 1977; APA 1987; IOM 1987; WHO 1978).

Research evidence in support of the dual clinical classification of alcohol abuse and dependence is found in recent studies on the outcome of alcoholism treatment (Edwards et al. 1988), the classification of drinkers (Morey et al. 1984), and the course of problem drinking in patients with affective disorders (Hasin et al. 1989). Two formal diagnostic systems which reflect contemporary clinical and research knowledge, the *International Classification of Diseases* of the World Health Organization (WHO 1978) and the *Diagnostic and Statistical Manual of Mental Disorders* of the American Psychiatric Association (APA 1987) now employ definitions that differentiate a nondependent problem drinking condition from alcohol dependence.

Implications for Prevention and Treatment

Any drinking that produces a problem, whether social or medical, mild or severe, is important to prevention and treatment. Included are problems associated with single bouts of high-risk alcohol consumption by any drinker, as well as problems associated with continued consumption by those whose drinking behavior may be clinically defined as alcohol abuse or dependence. Alcohol abuse and alcohol dependence result in undesirable outcomes that are tangible and serve as evidence to the individual and to others that alcohol use has become problematic.

The differentiation between alcohol abuse and dependence has important clinical implications.

For some nondependent alcohol abusers, drinking patterns may be modified simply by exhortations or by societal sanctions; for others, specific interventions aimed at modification of drinking behavior are appropriate (Miller and Hester 1986; Marlatt 1988). Thus, early identification of problem drinkers and intervention efforts involving such strategies as brief counseling, training, and advice are of considerable interest. Although research is not extensive, some evidence of the effectiveness of minimal interventions with certain nondependent problem drinkers has been provided (Chick et al. 1985; Elvy et al. 1988; Miller et al. 1988).

For alcohol-dependent persons, exhortations and sanctions are insufficient, and the goal of modified drinking inappropriate. The appropriate treatment goal for these persons is abstinence (Miller and Hester 1986; Nathan and Skinstad 1987). To this end, a range of treatment options is available, including pharmacologic interventions, psychotherapy and counseling, Alcoholics Anonymous, and a variety of behavioral training programs. Research on the effectiveness of various alcoholism treatment approaches has improved knowledge about the effectiveness of group therapy (Oei and Jackson 1984), spousal involvement in alcoholism treatment (O'Farrell et al. 1985), marital therapy (McCrady et al. 1986), social skills training (Eriksen 1986), and Alcoholics Anonymous (Emrick 1987).

The effectiveness of various pharmacologic agents has been investigated, including agents used in the medical treatment of the alcohol withdrawal syndrome (Liskow and Goodwin 1987) and agents that foster sobriety by interfering with the metabolism of alcohol, thereby producing a noxious reaction when alcohol is ingested (Fuller et al. 1986; Sereny et al. 1986). Distinguishing between alcohol abusers who are dependent and those whose problem drinking is not accompanied by dependence is necessary so that decisions about the most suitable intervention can be made.

Alcohol-dependent persons do not constitute a homogeneous group. Important aspects of heterogeneity among alcohol-dependent persons include highly varied psychiatric comorbidity (Hesselbrock 1986) and differences in personality, life experiences, family characteristics, and social status (Mendelson and Mello 1985). Another important aspect of heterogeneity involves late versus early onset (Blane 1979). The idea that great variation exists among alcoholic individuals is not new: Jellinek (1960) described five "species" of alcoholism having different manifestations. Two distinct types of alcoholism that have been identified (Cloninger 1987) will be discussed later in this chapter.

Knowledge of the differences among alcohol-dependent persons is important because research has shown that alcoholism treatment methods are differentially effective according to patient characteristics. McLellan et al. (1983) found that alcohol-dependent patients who were matched to specific treatments were more motivated during treatment and experienced more positive outcomes regarding employment, legal and family problems, medical status, and other drug use following treatment than unmatched patients. More recently, Kadden et al. (in press) found that following inpatient alcoholism treatment, aftercare involving training in coping skills produced more favorable drinking-related outcomes in patients high in sociopathy or psychopathology, whereas treatment aimed at exploring interpersonal style was more effective with those lower in sociopathy. Accordingly, there is considerable interest in research involving patient-treatment matching.

Prevention activities are directed at drinkers in general, at problem drinkers, and at those at risk for the development of problematic drinking. Prevention strategies attempt to avert the adverse effects of single bouts of drinking and to mitigate the effects of long-term abusive drinking (Holder 1988; Hingson et al. 1987). Prevention research investigates the effectiveness of approaches focused on individuals, such as educational efforts and health promotion programs (Moskowitz 1989; Rootman 1985; Hansen et al. 1988); approaches focused on the environment affecting drinkers (Rush et al. 1987; Blose and Holder 1987; Wagenaar 1986), including enforcement of drunk-driving laws (Hingson et al. 1988; Klitzner 1989) and public policies governing price and alcohol availability (Coate and Grossman 1987; Grossman et al. 1987); and approaches involving the interaction of individual and environmental approaches, such as server intervention programs (Saltz 1987, 1989; McKnight 1987; Geller et al. 1987).

Etiology

Both alcohol abuse and alcohol dependence arise as a result of different, complex, and as yet incompletely understood processes. Research has produced evidence that both genetic and environmental factors contribute to alcoholism, and the interaction of genetics and environment is emerging as a fundamentally important issue in the etiology of alcohol problems. Some forms of alcohol dependence are highly heritable, while others are less so; there are also instances of alcohol dependence without obvious genetic involvement (Cloninger et al. 1981). Notwithstanding the limitations of current knowledge and the clear need to pursue research on etiology, some statements about causation can be made.

Even though the mechanisms of genetic transmission are unknown, evidence of genetically transmitted vulnerability for alcoholism exists. Much of this evidence has arisen from adoption studies (Cloninger et al. 1981; Goodwin et al. 1973; Bohman et al. 1981), but additional support for potential genetic contributions is found in research on markers of inherited susceptibility (Tabakoff et al. 1988; Porjesz and Begleiter 1979, 1985; Schuckit et al. 1987; von Knorring et al. 1987; Moss et al. 1989; Crabbe et al. 1988) and in research involving animal models (Crabbe et al. 1985; Lumeng and Li 1986; Gatto et al. 1987a,b). Recent twin studies suggest that the interaction between genetic and environmental influences is implicated in certain drinking behaviors (Heath and Martin 1988; Heath et al. 1989).

Such psychosocial factors as cultural and group norms and peer influences (Jessor and Jessor 1975; Zucker and Noll 1982) and expectancies about alcohol's effects (Marlatt et al. 1988; Marlatt 1987; Zinberg 1984; Goldman et al. 1987) influence drinking behavior. Likewise, subjective experiences related to the pharmacologic effects of alcohol (Sher 1985; Levenson et al. 1987; Hunt 1987a,b), most notably its euphoriant and anxiety-reducing effects, are reinforcing for some drinkers. The effects of the early home environment, including family influences, on drinking behavior and the development of alcohol dependence have been explored, as has the relationship of childhood adjustment problems to later alcoholism (McCord 1988; Werner 1986; Drake and Vaillant 1988; Zucker and Gomberg 1986). Age-related drinking patterns (Fillmore 1987a,b; Fillmore and Midanik 1984; Donovan et al. 1983) and generational secular trends (Reich et al. 1988) have also been noted.

In describing two subgroups of alcohol dependence, Cloninger (1987) showed one way in which genetic and environmental influences may interact to produce alcoholism. One subgroup (type 2, male-limited) has a high genetic penetrance from father to son and minor environmental association. Onset typically occurs before the age of 25 with drinking patterns characterized by persistent consumption accompanied by aggressive behavior and involvement with the police. The other subgroup (type 1, milieu-limited) has a more complex etiologic picture in terms of the interplay of genetic and environmental influences. Onset of type 1 alcohol dependence typically occurs after the age of 25 with a drinking pattern characterized by guilt and periods when control over drinking is severely diminished. Personality characteristics related to three traits—novelty seeking, harm avoidance, and reward dependence—are thought to differentiate the types and to represent key differences in the processes by which individuals respond to the environment (Cloninger 1987).

A perspective on the integration of genetic and environmental findings about vulnerability to alcoholism is also found in the work of Tarter et al. (1985). In this view, temperament trait deviations underlie characteristics found to be associated with alcohol dependence in males, and these deviations are related to neurological deficits in frontal-midbrain functioning. The temperament perspective is useful because it suggests environmental factors that modify biological predisposition; for example, the match between the child's inherent temperament and the childhood home environment may serve to modify the risk for alcoholism (Tarter et al. 1985).

Genetic factors may also interact with environmental influences in the development of certain patterns of alcohol consumption and alcohol abuse, but the etiologic loading of genetic versus environmental influences may vary from individual to individual (Cloninger 1987).

It is important to note that genetic predisposition does not imply predestination or inevitability. Many persons having family histories indicative of risk do not develop alcohol dependence since it is the interaction of genetic and environmental factors that define vulnerability. Thus, even if facilitative genes are inherited, they may not be expressed in the absence of provocative environmental factors. Although it is estimated that one-third of alcoholics have one or more parents who are also alcoholic (Cotton 1979), less than half of children of alcoholics develop drinking problems, and only a portion of these develop alcohol dependence (Zucker 1986). In an analysis of data from a national survey of drinking practices, Harford et al. (1987–88) found that, among males, 15 percent of those with an alcoholic parent reported one or more symptoms of alcohol dependence; among females, 9 percent. However, the number of dependence symptoms was greater among adult children of alcoholics of both genders than among persons with negative family histories (Harford et al. 1987-88). Thus, researchers are particularly interested in identifying the factors associated with resistance to the development of dependence because those at risk for alcohol dependence can make critical lifestyle decisions about drinking that are protective, in much the same fashion that those at risk for diabetes can make risk-reducing decisions about diet, exercise, and weight.

Contemporary understanding of alcohol abuse and alcohol dependence incorporates evidence from studies representing different research traditions. Biological factors, including heredity, play a key role, and the impact of psychological and social factors on drinking behavior may be differentially relevant at different developmental stages (Zucker 1986; Zucker and Gomberg 1986). In the formulation of an integrated explanatory model, consideration must be given to continuities that occur across the life span, as well as to breaks in continuity that occur over time (Zucker 1986), and a synthesis of knowledge about biological factors and data concerning social context and cognitive factors associated with drinking behavior must occur (Wilson 1987).

Alcohol Dependence as a Disease

Alcohol dependence, like hypertension, diabetes, and coronary artery disease, may be characterized as a biologically based disease in which a genetic predisposition is activated by environmental factors. It has been noted that alcoholism fits within the pattern of most of the other major chronic diseases that are the consequence of the accumulation of environmental factors over time in genetically susceptible persons (Williams 1988). For example, hypertension has been shown to be strongly genetically linked, yet to conclude that genetic factors alone are causal would be erroneous, because such environmental factors as salt intake and smoking may play important etiologic roles (Williams 1988).

Alcohol dependence is not an infectious disease or a disease in which cells multiply wildly. Rather, in alcohol dependence, biology and behavior interact in complex ways. In this context, alcohol dependence may represent the end result of an interactive process involving many different social and psychological factors in persons who are physiologically vulnerable (Tarter et al. 1985).

To be classified as a disease, a disorder has an identifiable cluster of symptoms that predicts a course and outcome. In terms of meeting these criteria, alcohol dependence is not different from other biologically based diseases. Alcohol-dependent persons may experience predictable withdrawal syndromes, severe physical effects resulting from abstinence, and craving, intense, overwhelming compulsions to drink. Withdrawal and craving may contribute to the development of impaired control over drinking. In addition, alcohol-dependent persons develop tolerance to alcohol, that is, a need for increased quantities of alcohol to achieve a pharmacologic effect (Tabakoff et al. 1982).

The fact that the line between severe alcohol abuse and alcohol dependence is sometimes difficult to draw does not interfere with the recognition of alcohol dependence as a disease, for differential diagnosis of borderline cases is problematic in many other medical conditions from diabetes to hypertension. Similarly, the occurrence of spontaneous remission in some alcoholic individuals is not inconsistent with this recognition, for poorly understood remissions occur in many disease states.

Unlike most nonproblem drinkers, alcohol-dependent persons may lack internal signaling mechanisms that allow them to regulate their alcohol intake and judge their relative intoxication (Lipscomb and Nathan 1980). Indeed, because alcohol is a source of calories as well as a drug, disturbance in appetite-controlling mechanisms may be implicated in alcohol dependence.

The existence of impaired control in alcohol-dependent individuals has at times been challenged, but research evidence continues to support its occurrence. Impaired control, difficulty in restricting alcohol intake, is associated with craving, which may represent a state in which physical dependence is accompanied by the development of a conditioned response to environmental, social, or emotional cues (Ludwig and Wikler 1974). Alternatively, craving may result from the expectation that alcohol consumption will produce desirable consequences, especially in certain social contexts among those having limited coping skills and little confidence in their ability to resist (Marlatt 1985; Wilson 1987).

A number of researchers have studied craving for alcohol, alcohol-seeking behavior, and cognitive factors associated with these phenomena. For example, Ludwig, Wikler, and Stark (1974) found both craving for alcohol and behavior aimed at acquiring alcohol to be determined by the interaction of environmental cues (e.g., sight and smell of alcohol) and a small initiating alcohol dose. Marlatt et al. (1973), comparing alcoholics and social drinkers, found that the amount consumed was determined by the expectation of beverage content rather than actual content, and that both drinker types drank more when they thought the mixture they were given contained alcohol. Another study (Cooney et al. 1987) found that when alcoholic and nonalcoholic subjects were exposed to alcohol (but did not drink it), alcoholics reported more physical symptoms than nonalcoholics; among alcoholic subjects, confidence in their ability to resist drinking was significantly diminished following exposure to alcohol. Increasing knowledge about cognitive factors associated with craving has important implications for treatment and relapse prevention interventions (Marlatt 1985; Wilson 1987; Monti et al. 1988).

Summary

Alcohol abuse and dependence are serious problems that affect about 10 percent of adult Americans. Adverse social and medical consequences of abusive drinking arise as a result of single bouts of drinking as well as from longer term effects of alcohol consumption. A minimum of 3 out of 100 deaths in the United States can be attributed to alcohol-related causes. Adverse consequences may affect not only the drinker but also others with whom the drinker comes in contact, and the economic cost is high.

Two distinct forms of problematic drinking, alcohol abuse and alcohol dependence, have been identified. Alcohol abuse involves persistent patterns of heavy alcohol intake in which health consequences and/or impairment in social functioning are associated. Alcohol dependence is differentiated from alcohol abuse on the basis of such manifestations as craving, tolerance, and physical dependence that result in changes in the salience of drinking in one's life and in impairment in the ability to exercise restraint over drinking.

Any drinking that causes a problem, whether social or medical, mild or severe, is significant to prevention and treatment. Prevention activities are directed at drinkers in general, at problem drinkers, and at those at risk for the development of problematic drinking. Prevention strategies attempt to avert the adverse effects of single bouts of drinking and to mitigate the effects of long-term abusive drinking.

The differentiation between alcohol abuse and alcohol dependence has important clinical implications, since different goals and intervention methods are used. For some nondependent alcohol abusers, interventions aimed at modifying harmful drinking patterns are appropriate. Early identification of such individuals and intervention methods involving advice, brief counseling, and training have been employed. For alcohol-dependent persons, the appropriate treatment goal is abstinence, and a range of treatment options, including pharmacologic interventions, psychotherapy and counseling, Alcoholics Anonymous, and a variety of behavioral training programs are used. Both alcohol abuse and dependence arise as a result of different complex and as yet incompletely understood processes. It is known, however, that the interaction of genetic factors with psychological and social factors is implicated in the cause of alcohol dependence, which, like coronary artery disease, diabetes, and hypertension, is a biologically based disease in which genetic predisposition interacts with environmental factors. Genetic predisposition does not imply predestination, however, and research aimed at the identification of factors associated with resistance is of interest.

Psychological and social factors including cultural and group norms, peer influences, expectations about alcohol's effects, subjective experience related to alcohol's actual pharmacologic effects, and factors in the home environment influence an individual's drinking behavior. In addition, age-related drinking patterns and generational secular trends have been observed.

Alcohol-dependent persons represent a heterogeneous population, in terms of psychiatric comorbidity, and differences in genetics, personality, background, family characteristics, and social status. There is considerable interest in identifying characteristics that have treatment relevance since there is evidence that alcoholism treatment is more effective when the specific treatment regimen is matched to characteristics of the patient. In addition, two clinical subtypes of alcoholics have been identified that differ in terms of the interaction of genetic and environmental influences and in clinical manifestations.

Alcohol research has provided the foundation of knowledge on which an understanding of key issues regarding the causes, prevention, and treatment of alcohol abuse and alcoholism is built. Still, much is to be learned and many questions are yet to be answered. A particularly rich source of new knowledge and potentially dramatic advances in understanding is future research on alcohol abuse and alcohol dependence that draws from both biological and behavioral sciences. In science, boundary areas between disciplines represent unique opportunities for cooperation and exciting prospects for advancement.

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Chapter II

Epidemiology

Introduction

During the 1980s we have seen a gradual but consistent downturn in per capita alcohol consumption in the United States after two decades of steady increases. The change could simply represent a temporary plateau in the long upswing that characterized consumption during the 1960s and 1970s. However, parallel declines have been noted in many other countries, particularly in the industrialized West, and there have been slight decreases in some indicators of alcohol abuse such as mortality from liver cirrhosis and from alcoholism. Further, population surveys indicate increases in abstention, especially among men, and decreases in alcohol consumption among adolescents. These changes may lend support to the view that the drop in alcohol consumption over the past few years may presage a "drier" era. On the other hand, there is evidence of an increasing proportion of heavy drinkers among young people in their twenties and a small increase in the prevalence of dependence problems—findings that underline the importance of continued surveillance.

With a view toward further examination of patterns and trends in alcohol use and abuse, this chapter describes recent findings related to alcohol consumption, alcohol-related morbidity and mortality, and adverse social consequences of alcohol use and abuse, both in the general population and in several population subgroups: women, adolescents and young adults, older adults, the homeless, and racial and ethnic minorities.

Consumption

Per Capita Consumption

The amount of alcohol consumed in the United States is estimated on the basis of alcohol sales in each State as determined from tax receipts, sales in State-controlled stores, and/or reports from beverage industry sources. These overall statistics do not include estimates of home production, illegal production, breakage, or untaxed alcohol brought in by tourists. Apparent per capita consumption is determined by dividing total alcohol, derived from sales, by the total population aged 14 or older. The term "apparent" is used because these estimates artificially attribute average consumption to all persons in this population, regardless of their actual consumption.

Per capita consumption is expressed in gallons of pure alcohol calculated by multiplying total gallons of each beverage type by a conversion factor (0.045 for beer, 0.129 for wine, and 0.411 for spirits). In 1987, apparent per capita consumption of alcohol was 2.54 gallons of pure alcohol, the lowest level since 1970 (NIAAA 1989). Nevertheless, alcohol is used by more Americans than any other drug, including cigarette tobacco. In a U.S. household survey of persons aged 12 and over, 73.4 percent reported drinking alcohol in the past year; 36.2 percent reported smoking cigarettes (NIDA 1988). Figure 1, illustrating the pattern of per capita consumption from 1977 through 1987, shows the peaking of total alcohol consumption in 1980 and 1981 with the subsequent continuing decline.

The major component of the decrease was the large decline in consumption of spirits, which dropped to 0.83 gallons of pure alcohol per capita in 1987—the lowest consumption level for spirits since 1958. Beer consumption remained at the 1986 level of 1.34 gallons per capita, the lowest level of beer consumption since 1978 and 4 percent lower than the 1981 peak level of 1.39 gallons (see fig. 2). For the first time in more than 10 years, wine consumption did not increase.

One suggested reason for the steady decline in alcohol consumption since 1981 is an increase in public awareness of the risks associated with alcohol use and abuse. Changing demographics may be another reason, as the proportion of the population that is over age 60 continues to increase; alcohol consumption in this age group is relatively low. The increasingly conservative cultural climate that has prevailed during the 1980s, with associated decreases in the social acceptability of heavy drinking, could be another factor. Tastes appear to have turned away from distilled spirits and toward beverages with lower alcohol content. For example, wine coolers, which did not exist in 1982, accounted for one-fourth of total wine consumption in 1986 (NIAAA 1988b). Decreases in alcohol consumption may also be related to increasing concern with overall health and fitness as exemplified by current trends toward reductions in smoking and increased emphasis on nutrition and exercise.

Although estimates of consumption levels for other countries are somewhat variable (Horgan et al. 1986; PGD 1987), apparent per capita consumption began to level off in most industrialized countries except the United States in the mid-1970s, and by the mid-1980s many were experiencing declines. Of 25 countries surveyed between 1979 and 1984, nearly two-thirds experienced declines or stability in consumption (Horgan et al. 1986) (see fig. 3). Only four of the nine countries where consumption increased had rates of increase greater than 1 percent. In contrast, consumption in some of the developing countries has continued to increase (Hilton and Johnstone 1988).

Geographic Differences

Table 1 lists the total apparent per capita alcohol consumption for the 50 States and the District of Columbia in 1977 and 1986 and ranks them by 1986 decile. These figures should be interpreted with caution because they do not necessarily reflect true consumption levels of

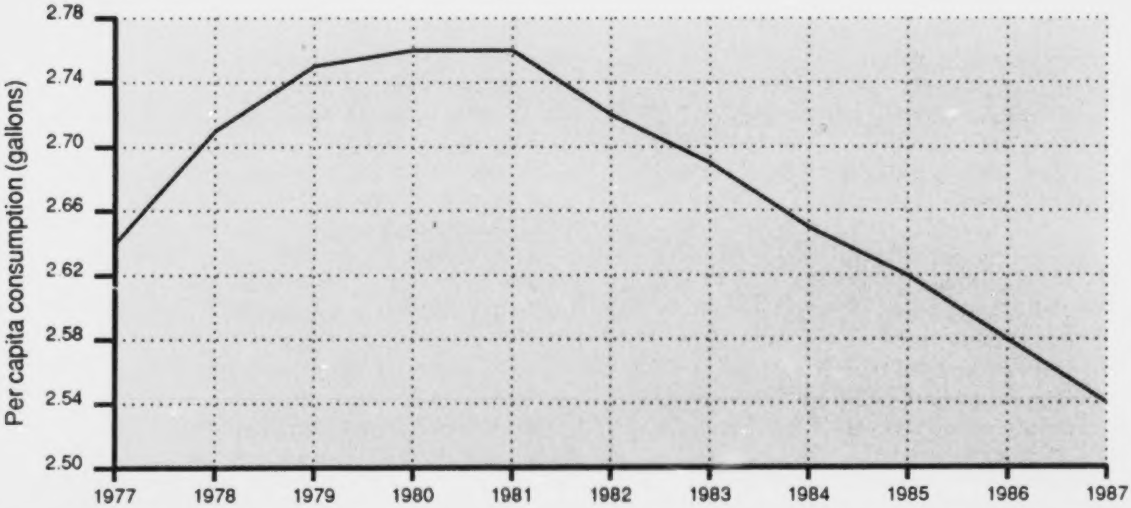


FIGURE 1. Apparent U.S. per capita consumption of pure alcohol, 1977–1987.
SOURCE: NIAAA 1989.

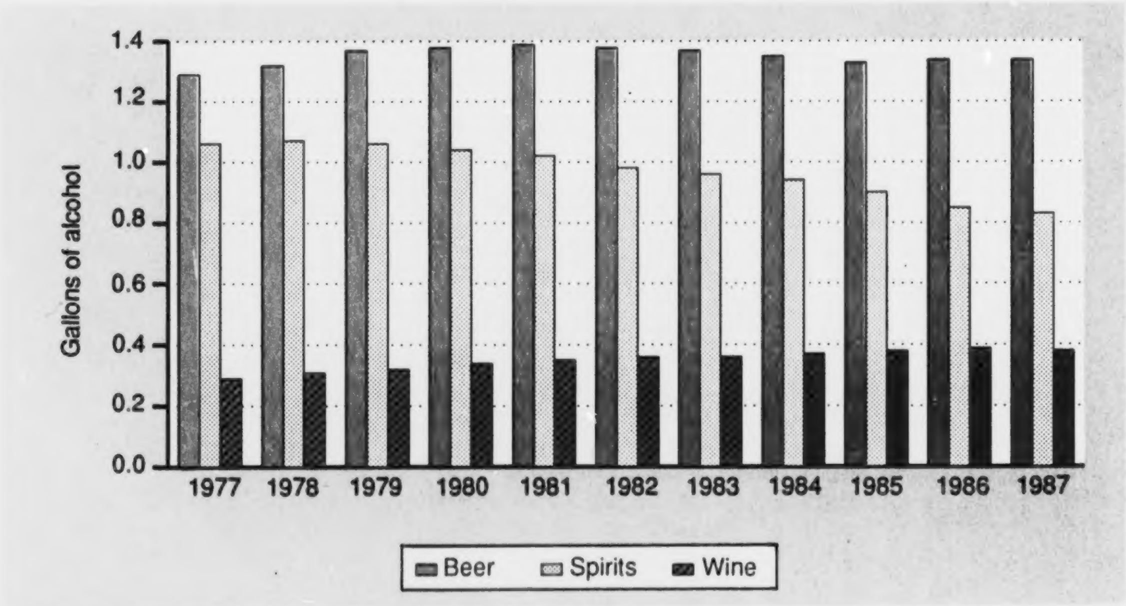


FIGURE 2. Apparent U.S. per capita consumption of beer, wine, and spirits, 1977–1987.
SOURCE: NIAAA 1989.

State residents. For example, consumption in the District of Columbia is affected both by a high level of tourism and by the fact that residents of nearby Virginia and Maryland take advantage of the District's lower alcohol taxes. A high proportion of Nevada's 1 million residents are Mormons and are therefore more likely to be abstainers; however, as a center for conventions and tourism, the State is visited by approximately 26 million people per year.

The State decile rankings remained fairly consistent between 1977 and 1986. Although many States have experienced substantial increases or decreases in apparent per capita consumption, there has been little change in their relative rankings. Changes in per capita consumption in the 50 States and the District of Columbia between 1977 and 1986 are illustrated in figure 4, which shows the greatest decreases in the District of Columbia, Hawaii, Montana, Nevada, New Hampshire, West Virginia, and Wyoming, and the greatest increase in Virginia.

When the States are grouped by U.S. census region as shown in table 2, it is apparent that both per capita consumption and numbers of abstainers differentiate the regions in terms of relative "wetness" or "dryness" (Hilton 1988b). Per capita consumption is highest in the wetter Pacific and New England States. However, if consumption is calculated for drinkers only (excluding abstainers), the highest consumption per drinker is found in the drier Mountain and southern regions. Although there are fewer drinkers in these drier States, it appears that they consume more alcohol per capita than drinkers in the other regions. However, it is possible that some drinkers in the drier regions may report themselves to be abstainers because of prevailing social attitudes toward drinking.

Although there were few important indications of regional differences in the prevalence of heavy drinking, men in the drier regions experienced significantly more alcohol-related problems, particularly in the areas of belligerence, accidents, problems with police, and problems with friends or spouse (Hilton 1988b). Again, this difference could be a consequence of the less tolerant attitudes prevalent in a relatively abstinent social milieu.

Patterns of Consumption

Drinking patterns and consumption levels are estimated on the basis of individual responses to questions in general population surveys. These surveys may differ in the wording of questions, and thus the information elicited concerning drinking quantity and frequency may not always be comparable. However, these studies do provide valuable information on overall drinking

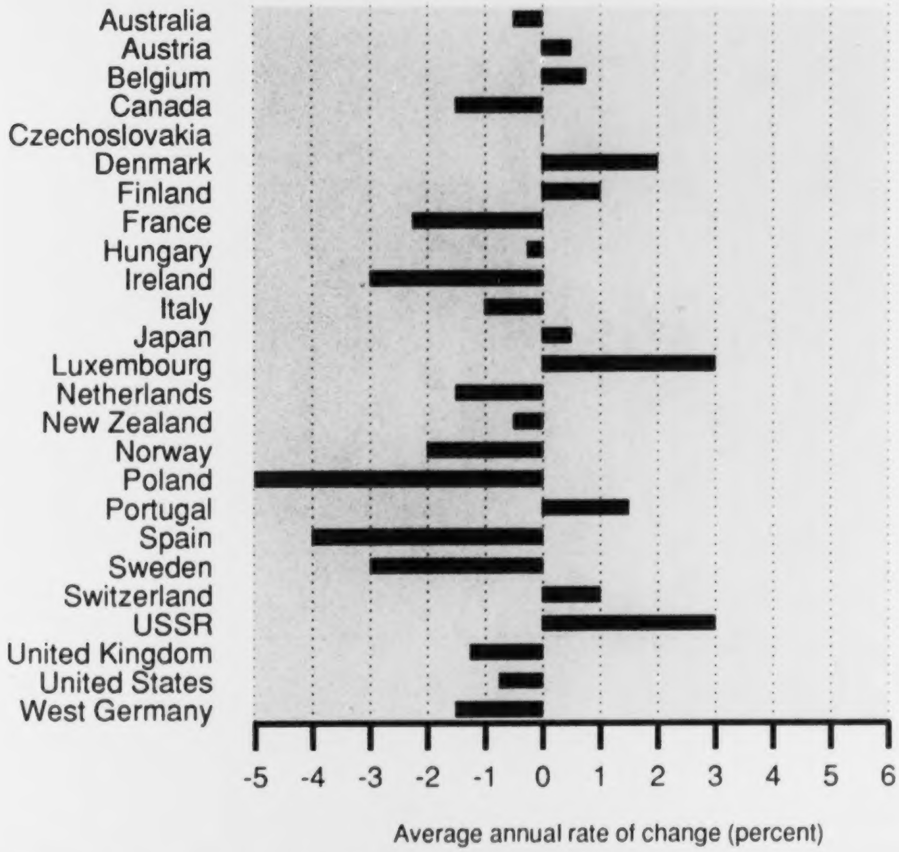


FIGURE 3. Average annual rate of change (percent) in per capita alcohol consumption for 25 countries, 1979–1984.
SOURCE: Horgan et al. 1986.

patterns and on changes and trends in these patterns.

Probably the most important differences between surveys are in the construction of typologies of drinking behavior (Room in press). One system of classifying drinkers is based on the average daily quantity of alcohol consumed (Hilton 1988d; Malin et al. 1986; Williams et al. 1986; S. Wilsnack 1987). Another system combines quantity consumed per occasion with drinking frequency (Cahalan et al. 1969). A variation of this system, designated "volmax," combines volume of monthly intake with maximum amount consumed per occasion (Hilton and Clark 1987). Knupfer (1987a) combines frequency of drinking (daily, weekly, or less than weekly) with the frequency of consuming specific amounts (from 1 or 2 drinks up to 12 or more). This system permits the evaluation of quantity and frequency both separately and in combination. A category for the frequency of getting drunk may also be included (Hilton 1988a; Knupfer 1984, 1987a,b).

Two surveys that included identically worded questions, and thus provided a basis for valid comparison, examined drinking patterns and drinking problems over a 17-year span from 1967 to 1984 (Hilton and Clark 1987). The study found few significant changes in reported consumption patterns during this 17-year period, except for a small increase in the proportion of abstainers (from 29 percent to 32 percent). Among men, the increase in abstention rates was statistically significant.

A comparison of results from 11 different surveys conducted during the 20 years from 1964 to 1984 provided a greater number of data points but at the cost of diminished comparability (Hilton 1988d). This study also showed stability in overall drinking patterns, consistent with findings of Hilton and Clark (1987). The 1988 study (Hilton 1988d) used higher cutpoints to define

TABLE 1. Apparent per capita alcohol consumption for the 50 States and the District of Columbia, 1977 and 1986, with decile rankings for 1986

	Per capita consumption (gallons)		Decile
State	**1977**	**1986**	**(1986)**
Alabama	1.96	1.91	9
Alaska	3.31	3.52	1
Arizona	3.10	3.15	2
Arkansas	1.65	1.64	10
California	3.25	3.12	2
Colorado	3.01	2.88	3
Connecticut	2.61	2.80	3
Delaware	2.91	3.13	2
District of Columbia	5.53	5.67	1
Florida	3.13	2.97	2
Georgia	2.47	2.44	6
Hawaii	3.23	2.89	3
Idaho	2.52	2.33	7
Illinois	2.87	2.68	4
Indiana	2.05	2.15	8
Iowa	2.17	2.05	9
Kansas	1.88	1.89	9
Kentucky	2.03	1.85	10
Louisiana	2.57	2.43	7
Maine	2.64	2.56	5
Maryland	3.05	2.76	4
Massachusetts	2.95	2.97	2
Michigan	2.71	2.57	5
Minnesota	2.65	2.56	5
Mississippi	2.05	2.05	9
Missouri	2.25	2.37	7
Montana	3.12	2.74	4
Nebraska	2.53	2.28	7
Nevada	6.84	5.07	1
New Hampshire	5.32	4.52	1
New Jersey	2.69	2.78	3
New Mexico	2.93	2.70	4
New York	2.74	2.55	6
North Carolina	2.05	2.16	8
North Dakota	2.62	2.40	7
Ohio	2.04	2.18	8
Oklahoma	1.98	1.81	10
Oregon	2.74	2.54	6
Pennsylvania	2.29	2.23	8
Rhode Island	2.93	2.87	3
South Carolina	2.49	2.50	6

TABLE 1. (continued)

State	Per capita consumption (gallons)		Decile
	1977	1986	(1986)
South Dakota	2.38	2.24	8
Tennessee	1.91	1.96	9
Texas	2.58	2.63	5
Utah	1.70	1.58	10
Vermont	3.44	3.18	1
Virginia	2.30	2.53	6
Washington	2.89	2.66	4
West Virginia	1.85	1.84	10
Wisconsin	3.31	3.16	2
Wyoming	3.31	2.64	5

SOURCE: NIAAA 1988b.
NOTE: Placement in the first decile indicates that a State ranks among the top 10 percent in total per capita consumption, placement in the second decile indicates the top 20 percent, and so on.

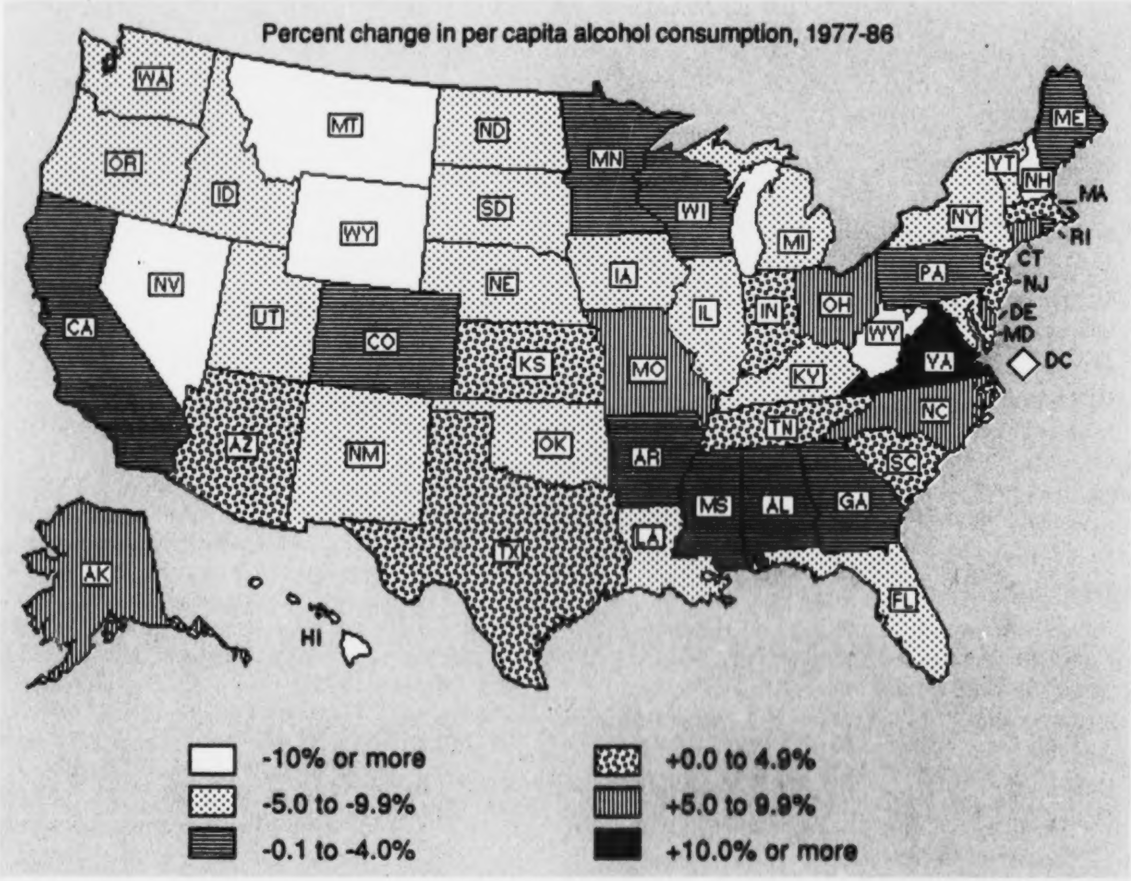

Percent change in per capita alcohol consumption, 1977-86
WA
OR
ID
MT
WY
ND
SD
NE
MN
WI
MI
IA
IL
IN
OH
PA
NY
VT
NH
ME
MA
RI
CT
NJ
DE
MD
DC
WV
VA
KY
NC
TN
SC
GA
AL
MS
LA
AR
MO
KS
OK
TX
NM
AZ
UT
CO
NV
CA
AK
HI
FL
☐ -10% or more
▒ -5.0 to -9.9%
▤ -0.1 to -4.0%
▒ +0.0 to 4.9%
▥ +5.0 to 9.9%
■ +10.0% or more

FIGURE 4. Trends in alcohol consumption: percent change in apparent per capita consumption of alcohol (gallons), United States, 1977–1986.
SOURCE: NIAAA 1988b.

TABLE 2. Distribution of apparent per capita alcohol consumption (in gallons of pure alcohol), percentage of abstainers, and apparent per-drinker consumption in the nine U.S. census regions, 1964, 1979, and 1984

	Apparent per capita consumption (gallons)			Abstainers (percent)			Apparent per-drinker consumption (gallons)		
Region	**1964**	**1979**	**1984**	**1964**	**1979**	**1984**	**1964**	**1979**	**1984**
Wetter regions									
New England	2.48	3.14	3.08	21	18	28	3.14	3.78	4.28
Mid-Atlantic	2.41	2.67	2.57	17	25	18	2.92	3.53	3.13
East North Central	2.26	2.67	2.57	25	29	27	3.04	3.75	3.52
West North Central	1.82	2.45	2.32	34	38	20	2.77	3.95	2.90
Pacific	2.55	3.38	3.09	27	16	26	3.47	3.99	4.18
Mean	2.30	2.86	2.73	25	25	24	3.07	3.80	3.60
Drier Regions									
South Atlantic	1.89	2.81	2.68	42	50	38	3.27	5.44	4.32
East South Central	1.01	1.95	1.93	65	66	56	2.87	5.48	4.39
West South Central	1.71	2.62	2.58	38	38	42	2.76	4.21	4.45
Mountain	2.08	3.29	2.96	42	38	38	3.58	5.31	4.77
Mean	1.67	2.67	2.54	47	48	44	3.12	5.11	4.48

SOURCE: Hilton 1988b.

heavy drinking than those used in the Hilton and Clark study, with the result that changes at the higher end of the drinking spectrum were revealed. For example, compared with Hilton and Clark (1987), Hilton (1988d) defined heavy drinking in terms of a higher number of drinks consumed per month, a greater frequency of consuming five or more drinks per occasion, and getting drunk at least once a week (a measure that was not considered in the 1964 survey). Using these criteria, Hilton (1988d) found increases in heavy drinking among men, particularly those aged 21 to 34, and also among women in the same age group. As guides for future research, these findings highlight the importance, stressed by Knupfer (1987b), of using cutpoints that are high enough both to differentiate the heaviest drinking levels and to detect patterns and changes at these levels.

Men are more likely than women to be drinkers and to be heavier drinkers. The hypothesis has often been advanced that drinking and heavy drinking have been increasing among women, resulting in a convergence of drinking patterns between men and women. Fillmore (1984), addressing this question in a cohort analysis, found overall consistency in women's drinking patterns for 1964, 1967, and 1979, with the exception of a shift toward more frequent heavy drinking in the younger cohorts. Women in their twenties in 1979, particularly those who were employed, had a higher rate of frequent heavy drinking than did earlier cohorts measured at the same age. These findings suggest the possibility that changes may be taking place currently among younger cohorts. Followup surveys are needed to trace the drinking patterns of these women as they age. Findings of this analysis are consistent with those of Hilton (1987b, 1988d), who also found stability in women's drinking patterns, with the exception of a similar increase in the proportion of heavy drinkers among younger women.

Temple (1987) analyzed surveys of college students in 1979, 1981, and 1984 and found that alcohol consumption decreased somewhat among both males and females during this time, but differences in drinking levels between males and females remained the same. Thus there had been no convergence in patterns of alcohol use between college-age men and women.

Results of a 1981 survey of women's drinking indicated that younger women were most likely to report frequent heavy drinking and repeated intoxication (R. Wilsnack et al. 1984). However, comparison of this survey with results of several earlier surveys showed that when only drinkers were compared, the greatest increase in the proportion of heavier drinkers was in the 35-to-49 age group. Overall, the 1981 survey results showed that although there is no evidence of any major increase in women's drinking, indications are that some of those who do drink may be drinking more heavily. The result could be future increases in alcohol-related problems among women.

As S. Wilsnack (1987) pointed out, perceptions that drinking patterns of men and women are converging, despite the lack of empirical evidence, may reflect in part a delayed social reaction to earlier changes in women's drinking (i.e., between World War II and the early 1970s). Another possible explanation for this perception of increased drinking by women may be the increased visibility of women's alcohol problems as more women seek treatment. Drinking patterns and problems among women are further discussed later in this chapter.

Alcohol-Related Morbidity

Alcohol use is associated with deleterious effects on virtually every part of the body. Chapter V provides a detailed description of the major diseases and disorders related to alcohol abuse and alcohol dependence.

The impact of alcohol abuse and dependence on the incidence and prevalence of disease is difficult to assess accurately, partly because of inadequate measures of alcohol consumption in many medical epidemiological studies. A major source of information on the extent of alcohol-related morbidity is the National Hospital Discharge Survey (NHDS), which provides an annual summary of data on discharges from short-stay community hospitals (NCHS 1989a). The NHDS recording system allows for the listing of up to six diagnoses in addition to the principal diagnosis for each patient, thus permitting estimation of the comorbidity (co-occurrence) of alcohol-related disorders with other disorders.

In 1985 there were approximately 27.4 million short-stay hospital discharges (excluding those related to pregnancy) among persons aged 14 and older. Approximately 1.1 million of these discharges (4 percent) involved an alcohol-related diagnosis, either with or without concurrent disorders. In nearly 600,000 (54 percent) of these cases, an alcohol-related disorder was the principal diagnosis. More than 68 percent of alcohol-related principal diagnoses were for alcohol dependence syndrome, 16 percent for chronic liver disease and cirrhosis, 9 percent for alcoholic psychoses, and 6 percent for nondependent abuse of alcohol. Males were three times more likely than females to have an alcohol-related diagnosis.

Almost half of alcohol-related morbidity in 1985 was secondary to other diagnoses. The discharge data revealed important associations between alcohol-related diagnoses and diseases and disorders of the liver, pancreas, digestive tract, respiratory system, nervous system, and cardiovascular system, as well as with drug abuse, mental disorders, injuries, accidental poisoning, infections, anemias, and malnutrition. Table 3 lists percentages of comorbidity for non-alcohol-related diagnoses that frequently are associated with an alcohol-related diagnosis. However, the degree of comorbidity is likely to be underestimated. For example, Towle et al. (1988) found that NHDS estimates of comorbidity for casualties (coded as accidents and injuries) for a 7-year period were relatively low, probably because of underreporting. (See chapter VII.)

The proportion of discharges that involved an alcohol-related diagnosis reported in the short-stay hospital survey, however, probably represents an underestimation of the extent of alcohol-related problems among hospitalized individuals. The survey included only hospitals where the length of patient stay was 1 month or less, and it did not include hospitals, such as Veterans Administration hospitals, that often treat multiproblem patients. Furthermore, data were obtained from hospital records; thus, underdiagnosis of alcohol problems would produce lower rates.

In this regard, a comprehensive hospital-based study (Moore et al. 1989) screened all newly admitted adult inpatients for alcoholism and

TABLE 3. Non-alcohol-related diagnoses frequently associated with an alcohol-related diagnosis, and percentage of comorbidity, short-stay hospital discharges, 1979–1984 (aggregated data)

Non-alcohol-related diagnosis	Percent with an associated alcohol-related diagnosis
Thiamine deficiency	66.2
Liver abscess and sequelae of chronic liver disease	55.6
Varicose veins (other than lower extremities, hemorrhoids, phlebitis, or other venous thrombosis)	49.5
Drug dependence	36.4
Spinocerebellar disease	28.6
Nondependent drug abuse	25.2
Hypothermia	22.8
Necrosis of the liver	19.8
Diseases of the pancreas	19.6
Personality disorders	19.6
Coagulation defects	16.6
Drug psychoses	15.7
Deficiency of B-complex components	13.3
Poisoning by psychotropic agents	12.2
Late effects of tuberculosis	11.8
Viral hepatitis	11.8
Gastrointestinal hemorrhage	11.6
Liver cancer (malignant neoplasm)	11.3
Pulmonary tuberculosis	10.5
Depressive disorder	10.3

SOURCE: Data from NCHS 1989a.

compared the rates obtained with physician identification of alcohol-related problems in the positively screened patients and in a random sample of the negatively screened patients. The overall prevalence of positive screenings was 25 percent, and the following department-specific prevalence rates for positive alcoholism screening were reported: psychiatry, 30 percent; medicine, 25 percent; surgery, 23 percent; neurology, 19 percent; and obstetrics/gynecology, 12.5 percent. Physicians involved in the treatment of the screened patients, however, significantly underdiagnosed alcohol abuse and alcoholism. Agreement between a positive screening and physician identification varied according to department. While there was agreement in two-thirds of the positive screenings on the psychiatric service, physicians treating surgical patients diagnosed an alcohol problem in about one-fourth of the positive screenings; physicians treating gynecology patients diagnosed an alcohol problem in less than 10 percent of women who screened positive. In terms of patient characteristics, Moore found that physicians were more likely to diagnose alcohol problems in positively screened individuals who were male, lower in socioeconomic status, and who acknowledged alcoholism as a problem. These findings underscore the need for physician education in the diagnosis of alcohol-related problems.

A large, comprehensive survey of psychiatric disorders in the general population found that about 13 percent of those surveyed had experienced alcohol abuse or dependence at sometime during their lives and nearly half of this group also had a psychiatric diagnosis (Helzer and Pryzbeck 1988). It is possible, however, that total pathology may be underestimated and prevalence of some disorders overestimated as a result of methodological problems. Although the diagnosis of alcohol dependence was five times more prevalent among men than among women, the association of alcoholism with other diagnoses was stronger in women; 65 percent of female alcoholics had a second diagnosis, compared with 44 percent of male alcoholics. Among alcoholics, 31 percent of females and 19 percent of males had diagnoses of drug abuse or dependence. Respective female and male prevalence rates for antisocial personality disorder were 10 and 15 percent; for phobic disorders, 31 and 13 percent; for major depression, 19 and 5 percent; for panic disorder, 7 and 2 percent; and for mania, 4 and 1 percent. Male alcoholics were only slightly more likely to have a diagnosis of major depression than men in the general population (5 versus 3 percent), but female alcoholics were much more likely to have this diagnosis (19 versus 7 percent). On the other hand, male alcoholics were almost four times more likely than males in the general population to have a diagnosis of antisocial personality disorder (15 versus 4 percent). The difference was even greater for women (10 versus 0.8 percent).

More than 1.4 million persons were treated in the United States for alcohol abuse and dependence in fiscal year 1987, as reported by the National Drug and Alcoholism Treatment Unit Survey (NDATUS). Three-fourths of those treated were male (NIDA/NIAAA 1989). Nearly one-third were between the ages of 25 and 34, and one-fourth were between 35 and 44. The great majority of admissions (72 percent) were white. Proportions of black and Hispanic admissions were somewhat higher than their respective proportions in the general population (15 percent and 10 percent of admissions, respectively). Asian-Americans, however, were substantially underrepresented among admissions (0.3 percent) and American Indians and Alaska Natives were overrepresented (3 percent).

A study of psychiatric comorbidity in patients who were in treatment for alcohol and/or drug problems showed that two-thirds had a current psychiatric disorder in addition to substance abuse (Ross et al. 1988). Lifetime prevalence of psychiatric diagnoses, excluding generalized anxiety, was found in 78 percent of those with alcohol-related disorders. Patients in treatment for alcoholism had lifetime prevalence rates of 42 percent for antisocial personality disorder, 31 percent for phobias, 30 percent for psychosexual dysfunction, 23 percent for major depression, 13 percent for dysthymia (a depressive disorder), 9 percent for panic disorder, and 8 percent for schizophrenia. Overestimation in some categories may have resulted, however, from the diagnostic methods used in the study. Further, comorbid patterns tend to differ in a treatment sample as opposed to a general population sample.

The Ross et al. (1988) study indicated that the likelihood of a patient having coexisting psychiatric disorders increased with increasing severity of alcohol (or drug) problems. This finding underlines the importance of psychiatric evaluation in all patients entering treatment programs for alcohol abuse. The comorbidity of psychiatric disorders with alcohol-related diagnoses is further discussed in chapter XI, and the problem of comorbidity (both psychiatric and medical) in the homeless is discussed later in this chapter.

Alcohol-Related Deaths

As discussed in the *Sixth Special Report to the U.S. Congress on Alcohol and Health* (USDHHS 1987), the true impact of alcohol abuse on mortality is difficult to assess. Alcohol-related conditions, particularly those that are contributing causes rather than direct causes of death, are substantially underreported on death certificates. Consequently, the 3 percent of deaths in the United States officially attributed to causes directly linked to alcohol represents a considerable underestimation (Van Natta et al. 1984–85). This may be due to reporting bias, lack of information on decedents' drinking histories, or both. It is also likely that alcohol involvement in deaths caused by motor vehicle crashes, drowning, falls, fires, and suicides is seriously underestimated. Mortality from these causes is further discussed in chapter VII.

Chronic liver disease and cirrhosis, the main chronic health hazard associated with alcohol abuse, was ranked as the ninth leading cause of death in the United States in 1986, causing more than 26,000 deaths in that year (NCHS 1989b). After the repeal of Prohibition in 1933, the chronic liver disease and cirrhosis mortality rate generally increased until it peaked at 15.0 deaths per 100,000 population in 1973 (see fig. 5). Since 1973, this rate has steadily decreased, and in 1986 it had dropped to 9.3 deaths per 100,000 population, the lowest rate since 1955. A similar phenomenon has been noted in Canada, where cirrhosis deaths declined by 25 percent between 1974 and 1984 (Mann et al. 1988). For a more detailed discussion of cirrhosis mortality, see chapter V.

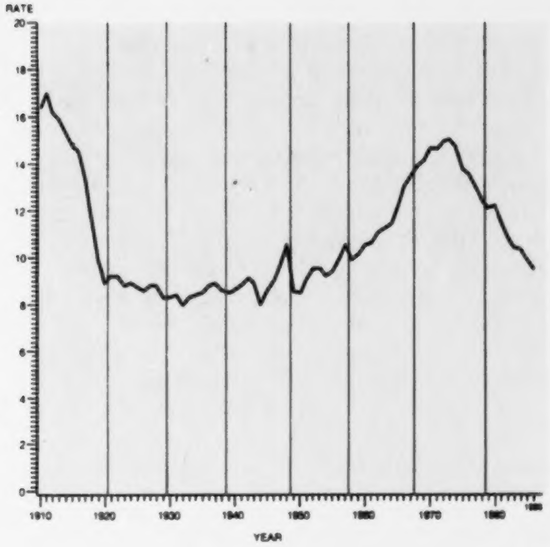


FIGURE 5. Age-adjusted mortality rates from chronic liver disease and cirrhosis, United States, 1910–1986 (rates per 100,000 population).
SOURCE: NCHS 1989b.

Alcohol Use Problems

Alcohol consumption is not a risk-free activity. In addition to enhancing one's vulnerability for alcohol-involved injuries and for alcohol-related illnesses and death, drinking can result in problems with one's family, friends, employers, and the police. For some drinkers, alcohol use and abuse can lead to alcohol dependence, which is associated with an inability to cut down on drinking, memory loss, morning drinking, impaired control over drinking, and withdrawal symptoms.

Prevalence of Drinking Problems

In reporting results of a 1984 national survey, Hilton (1987b) found that 7 percent of all drinkers had experienced moderate levels of dependence symptoms during the preceding year (i.e., they reported 3 or more of 13 indicators of dependence, such as impairment of control, morning drinking, and increased tolerance). Ten percent had experienced moderate levels of drinking-related consequences (i.e., they reported 4 or more of 32 consequences related to problems with spouse, job, police, or health). As would be expected, many drinkers reported both types of problem, and thus the categories are not mutually exclusive.

Problem levels were higher among men than among women. Among male drinkers, the proportion reporting at least a moderate level of problems was highest in the 18-to-29 age category for both dependence symptoms (14 percent) and drinking-related consequences (20 percent). The proportions dropped with increasing age, reaching respective lows of 5 percent and 7 percent among men aged 60 and older. Among female drinkers, the proportion reporting at least a moderate level of dependence symptoms remained stable at 5 to 6 percent from age 18 to age 49 and then dropped to 1 percent. For drinking-related consequences, however, the proportion reporting at least a moderate level of problems was relatively high in the 18-to-29 age group (12 percent) but dropped to 6 percent for women in their thirties and forties and was negligible for women aged 60 and older.

The demographic distribution of drinking-related problems appeared to match the distribution of heavy drinking, defined according to the frequency of heavy-drinking occasions (consumption of five or more drinks at a time at least once a week) (Hilton 1987a). This definition is in line with Knupfer's (1984, 1987b) contention that average or total alcohol intake is of little importance as a predictor of alcohol use problems and that the major predictive factor is the frequency of intoxication.

Survey respondents who were male, young, and single were more likely to report frequent heavy drinking and alcohol use problems (both dependence symptoms and drinking-related social and personal consequences) (Hilton 1987a). However, an analysis that examined only frequent heavy drinkers revealed little difference between the sexes in dependence symptoms and drinking-related consequences. Although significantly more single than married heavy drinkers had alcohol use problems, there were no significant correlations between problem levels and age at the high level of consumption. Frequent heavy drinkers with lower incomes and less education were more likely to report both dependence symptoms and alcohol-related consequences than were those at higher income and education levels.

Many of the questions in the 1984 survey were identical to questions asked in a 1967 survey. It was therefore possible to compare results of the two surveys to assess the nature and degree of change over the 17-year interval (Hilton and

Clark 1987). Hilton and Clark found higher rates of dependence symptoms among both men and women in 1984 than in 1967, but rates of other consequences remained stable over the 17-year period. Hilton (1988c) similarly compared data from the 1984 survey with data from a 1979 survey, examining changes over a shorter time period in order to take advantage of a greater number of comparable survey questions. There was a small increase in the prevalence of dependence problems among men, but not among women, and there was no increase in the prevalence of drinking-related consequences in either sex over the 5-year study period.

Chronicity of Drinking Problems

In addition to describing the prevalence of drinking patterns and problems across the life span, longitudinal studies also may reveal the ages at which drinking problems are likely to occur (incidence), to persist (chronicity), or to disappear (remission). Several such studies have examined the phenomenon of chronicity versus remission of alcohol problems in the general population (Fillmore 1987a,b; Fillmore and Midanik 1984; Hermos et al. 1988). Alcohol use problems among men in the general population tended to be transient, declining in both incidence and prevalence with increasing age after relatively high levels among the younger age groups (Fillmore 1987a). This decline suggested a high degree of spontaneous remission as drinkers moved into older age categories.

Fillmore and Midanik (1984) studied chronicity of both dependence problems and alcohol-related social problems as a function of age. They interviewed men in their twenties and men in their forties and, several years later, reinterviewed the same men. At the time of the first interview, the younger men reported more alcohol-related problems than the older men, but by the time of the second interview, their problem rates had decreased. Problem rates for the men in the older age group, on the other hand, showed little change over this period. These findings should be useful for estimating the true extent of chronic alcohol use problems in the population, at least among men. Estimates based on the number of persons in treatment, most of whom range in age from 35 to 60, would be too low; on the other hand, estimates based on the overall percentage of drinkers with problems would be too high because of eventual spontaneous remission among younger drinkers.

Fillmore (1987b) found distinctly different age-related patterns for alcohol problems among women. The onset of heavy drinking and drinking-related problems occurred later for women, whose problem rates peaked in the thirties rather than the twenties. Men reported higher levels of chronicity of problems in their forties and fifties, but women were more likely to report chronicity in their thirties. The emergence and persistence of alcohol problems thus occupied a more compressed timeframe for women. A further important difference was that women were likely to display much higher rates of remission than men across all decades of the adult life course.

In a study of predictive factors for reduction or cessation of drinking, Hermos et al. (1988) surveyed a group of men between the ages of 21 and 81 and interviewed them again 9 years later. For those who reduced their alcohol consumption but did not quit drinking, rates of alcohol-related problems did not change substantially between surveys even when there had been a marked decrease in alcohol consumption. Those who had quit drinking between the two surveys were more likely to have reported problems at the first survey than were other respondents. Conversely, drinkers who had problems at the first survey were far more likely to have quit drinking than were drinkers without problems at the time of the initial survey. Of all those who reported drinking problems at the first survey, fewer than half reported problems at the second. The level of chronicity was comparable to levels found by Fillmore (1987a,b; Fillmore and Midanik 1984), but this study, unlike Fillmore's, did not take into account age at the time of measurement. Age-related change and stability in drinking patterns are further discussed later in this chapter in the section on older adults.

Population Subgroups

Women

Fillmore (1984, 1987b) analyzed drinking patterns and problems among women on the basis of available survey data, although few alcohol studies before 1980 had focused specifically on women. Because women drink less than men and have relatively low rates of heavy drinking and of alcohol use problems, general population surveys provide little information on women's drinking problems. In an effort to compensate for this lack of data, in 1981 Wilsnack et al. conducted a national survey of women that oversampled moderate to heavy drinkers and those with histories of alcohol-related problems (R. Wilsnack et al. 1984, 1986; S. Wilsnack 1987; S. Wilsnack et al. 1986).

Although the survey found no major changes in women's drinking patterns during the preceding decade, it did identify several demographic subgroups with relatively high rates of drinking problems. High-risk groups related to employment included women who were unemployed and looking for work and those who were employed part time outside the home. With respect to marital status, those who were divorced or separated, or who had never married or were unmarried but living with a partner, were at greatest risk. Women in the last category had the highest rates of heavy drinking, drinking problems, and alcohol dependence symptoms of all the employment and marital status groups. Other high-risk groups were women in their twenties and early thirties and women with heavy-drinking husbands or partners.

In order to examine the correlations of risk factors with later drinking behavior, drinkers with and without alcohol-related problems in 1981 were reinterviewed in 1986 (S. Wilsnack 1987). This followup survey found that circumstances present in 1981 that were predictive of drinking problems or of increased consumption in 1986 included younger age, unemployment, having a heavy-drinking partner, living unmarried with a partner, low self-esteem, sexual dysfunction, and reproductive problems.

Because drinking may be both a cause and a consequence of physical illness, depression, marital or employment problems, and other stressful life experiences, it is necessary to study changes in drinking patterns over time in order to understand these relationships. R. Wilsnack et al. (1986) conducted a retrospective analysis of changes in women's drinking behavior in relation to depression and reproductive problems such as infertility, miscarriage or stillbirth, premature delivery, or having a child with a birth defect.

In this survey, only 25 percent of female drinkers reported that they had maintained a constant drinking level over time. Ten percent reported reductions in drinking with no intervening increases, and 23 percent increased their drinking levels with no reductions. The largest group, 42 percent, reported both increases and reductions in drinking during their lifetimes. For those women who reported experience with depression or reproductive problems and also with heavier drinking, time-ordered relationships were analyzed. For most of these women, heavy drinking was not an antecedent of depression or reproductive problems; rather, it began after the occurrence of the health problem, typically after a lag of several years. These findings suggest that although heavy drinking may lead to a variety of adverse reproductive consequences, the reverse may also be true: Problems with depression or reproductive disorders may precede and possibly contribute to the onset of heavy drinking.

The association of alcohol-related problems with women's changing roles across the life span was examined by Wilsnack and Cheloha (1987). Four age groups of female drinkers were analyzed with respect to marital, childrearing, and employment roles to determine whether certain role configurations increased the risk for developing drinking problems.

Female drinkers in the 21-to-34 age group were least likely to report alcohol-related problems if they were married and had a stable work role, either working full time for pay outside the home or working full time in the home without seeking outside work. Young women without children at home were more likely than those with children to report problems. Young single mothers with full-time, paid employment were consistently less likely to report alcohol-related problems than were young single mothers without full-time jobs.

In the 35-to-49 age group, the loss of family roles was closely associated with alcohol-related problems. Drinkers in this age group were more likely to report indicators of alcohol-related problems if they were divorced or separated or if they had one or more children but none currently living with them. Those who were married, had full-time jobs, and had children at home were the least likely to report drinking problems, indicating that the demands of multiple roles did not increase the risk of drinking problems among these women.

In the 50-to-64 age group, the risk of drinking problems was greatest for those who were married to drinking husbands, had children living elsewhere, and had no work role outside the home, and for those who were not currently married, had no children at home, and were either paid employees or students. Among women aged 65 and older, only 10 percent of the drinkers reported any indication of drinking problems.

Overall, the demonstrated relationships between alcohol use problems and the loss or lack of roles, together with the lack of evidence for multiple roles as a risk factor, suggest that drinking-related problems among women are related more to role deprivation than to role overload or to conflicts resulting from multiple roles.

In order to determine the relationship between women's drinking patterns and possible gender-role conflicts, women interviewed in the 1981 survey were studied with respect to traditionally gender-typed personality traits, personal values, and social roles (S. Wilsnack et al. 1985). Rates of heavy drinking and of drinking problems were strongly related to lowest scores on measures of personality traits reflecting an orientation toward selflessness and empathy and of traits focusing on marriage and children. Similarly, rates of heavy drinking and of problem consequences increased with increasing nontraditionality of social roles. The woman with the most nontraditional role configuration, according to these criteria, had never married or was separated or divorced, had no children, had an advanced degree, and was employed in a male-dominated occupation.

On the whole, this study showed that drinking levels and adverse consequences of drinking increased as women's gender-role orientations more closely approximated those traditionally associated with men. However, analysis of scores on a measure of psychological androgyny (i.e., having high levels of both traditionally feminine and masculine personality traits and personal values) revealed that women with high levels of psychological androgyny had lower drinking levels and fewer adverse consequences than did those with predominantly feminine or masculine traits and values.

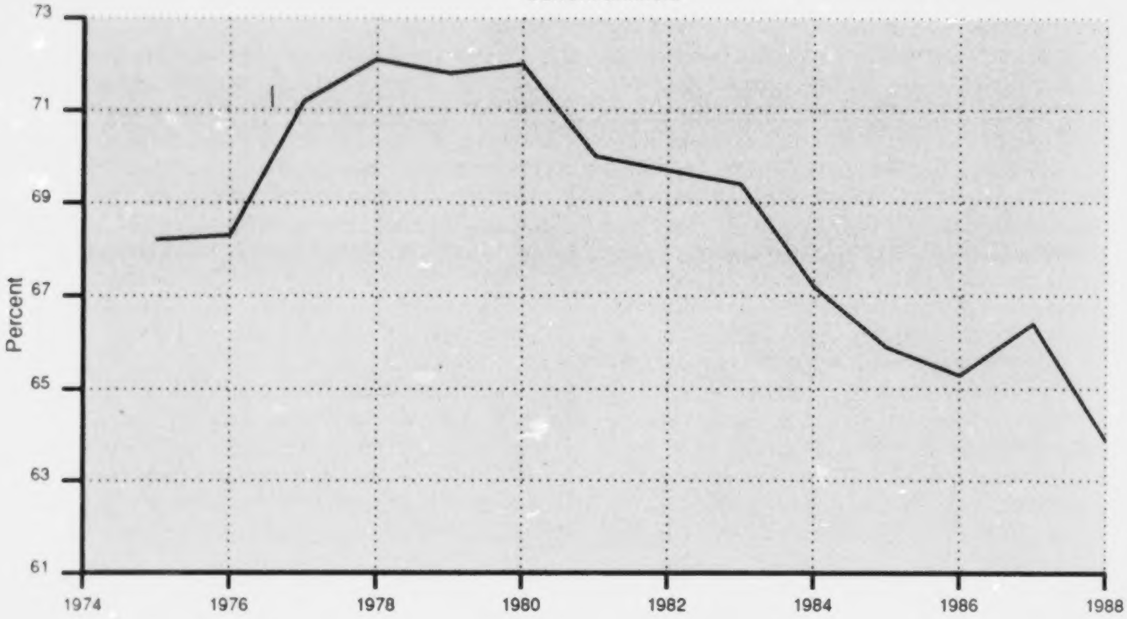
The relationship of gender to drinking and driving was examined by Peek et al. (1987), who analyzed 24 behavioral components of drinking and driving (drinking-driving history; crashes; driving origin and destination, such as places of entertainment, as opposed to home, stores, or workplace; and numbers of both child and adult passengers). Although female drinking and nondrinking drivers shared several behavioral similarities, the female drinking drivers were actually more similar in behavior to male drinking drivers than to female nondrinking drivers. Results of this study suggest that gender is probably not an important factor in explaining women's drinking-driving behavior or in differentiating between male and female drinking drivers.

A study of the demographic characteristics of women arrested for driving under the influence of alcohol over a 5-year period in a midwestern city also found close similarities between female and male drinking drivers (Shore, McCoy, Martin, and Kuntz 1988; Shore, McCoy, Toonen, and Kuntz 1988). Both groups consisted largely of single, highly intoxicated drivers in their twenties and thirties. The great majority of arrested women were single, divorced, or living with a partner (72 percent), compared with 28 percent who were married or widowed. Well over half (57 percent) were under the age of 30, and nearly one-third (31 percent) were unemployed. The percentage of women arrested increased each year, from 11 percent of the total in 1980 to 15 percent in 1984.

Adolescents and Young Adults

Every year since 1975, the Institute for Social Research at the University of Michigan has conducted a nationwide survey of approximately 17,000 high school seniors on drug and alcohol use and related attitudes. Since 1976, these annual surveys have also included followup studies. The most recent reports (Johnston et al. 1988, 1989) thus include data on young people between the ages of 18 and 30. These studies do not include high school dropouts, who constitute approximately 15 percent of the age group and who have prevalence rates for drug and alcohol use that are higher than those for students. However, careful examination of this problem led to the conclusion that failure to include dropouts as well as absentees in these surveys did not substantially affect estimates of incidence and prevalence of drug and alcohol use among adolescents (Johnston et al. 1988).

Complete results of the 1988 senior survey are not yet available, but it is apparent that there have been important recent changes in adolescent alcohol use (Johnston et al. 1989). Although the number of seniors who had tried alcohol at some time remained relatively stable at 92 percent, nearly all other indicators showed decreases in 1988. For the first time in several years, the proportion of seniors who were current drinkers declined significantly, from 66 percent in 1987 to 64 percent in 1988, down from a high of over 72 percent in 1978 (see fig. 6). The overall decrease from 1978 to 1988 was 11 percent. In 1987, 38 percent of seniors said that they had consumed five or more drinks at a sitting during the preceding 2 weeks, but in 1988 the proportion dropped significantly, to 35 percent, down from a high point of 41 percent in 1981 (see fig. 6). Just over 4 percent of seniors drank daily in 1988; this represents a 13-percent decline from 1987. In


Current drinkers

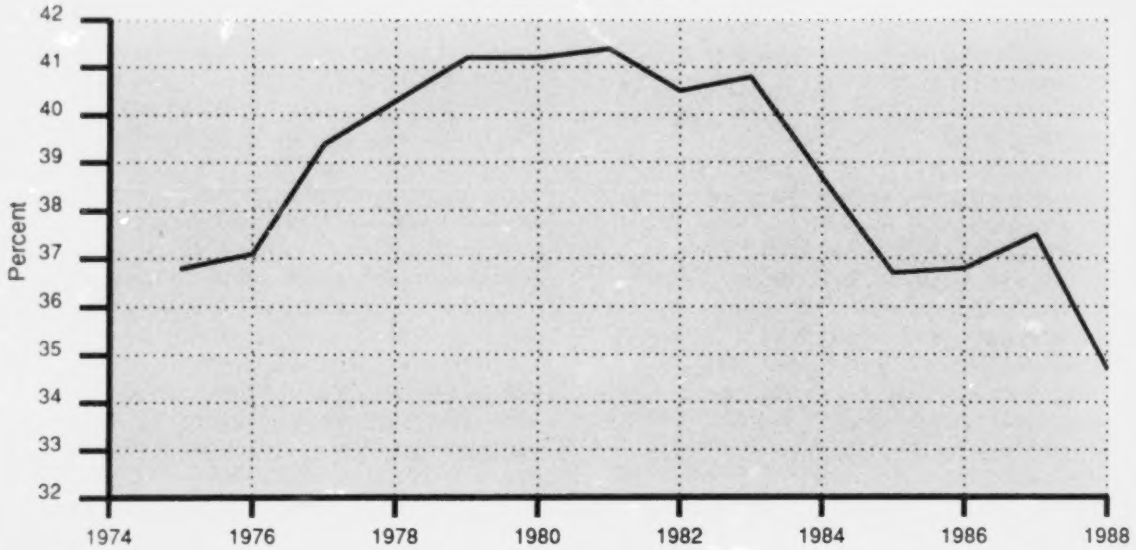

Occasional heavy drinkers

FIGURE 6. Percentage of high school seniors who were current drinkers (used alcohol in the past 30 days) and percentage who were occasional heavy drinkers (took five or more drinks at a sitting during the past 2 weeks), 1975–1988.
SOURCE: Data from Johnston et al. 1989.

1979, nearly 7 percent had reported daily drinking.

In 1987, seniors' attitudes and beliefs reflected a growing awareness of the potential hazards of both drug and alcohol use (Johnston et al. 1988). Between 1986 and 1987, percentages increased for those perceiving a great risk in trying alcohol (from 5 to 6 percent), taking one or two drinks nearly every day (from 25 to 26 percent), taking four or five drinks nearly every day (from 67 to 70 percent), and having five or more drinks once or twice each weekend (from 39 to 42 percent). Percentages also increased for students' personal disapproval of drinking practices: More than one-fifth disapproved of trying alcohol, three-fourths disapproved of daily drinking, and 92 percent disapproved of daily heavy drinking.

The decline in high school seniors' alcohol use paralleled concurrent declines in illicit drug use, indicating that there had been no displacement effect and that young people had not substituted alcohol for drugs or vice versa. Although these current declines are highly encouraging, they are not cause for complacency. The level of alcohol use by young people remains alarming: In 1987, two-thirds of high school seniors were current drinkers; more than one-third (and nearly half of males) indulged in occasional heavy drinking; nearly one-third did not perceive a great risk in having four or five drinks nearly every day; nearly one-third reported that most or all of their friends got drunk at least once a week; and nearly 10 percent had first used alcohol by the sixth grade (Johnston et al. 1988).

A statewide survey of more than 27,000 New York students in grades 7 to 12 (Barnes and Welte 1986) revealed alcohol use patterns similar to those found in the national survey of high school seniors. A large majority of the students were drinkers (71 percent), and males were more likely than females both to be drinkers and to be heavy drinkers. A series of four surveys in Ontario, Canada, of students in grades 7 to 13 found an equal proportion of drinkers (71 percent) (Smart et al. 1985).

The followup population of high school graduates maintained a pattern of alcohol use similar to that of the high school seniors, with somewhat higher levels of daily drinking and of drinking within the preceding month (Johnston et al. 1988). However, the proportion of graduates who consumed five or more drinks at a time during the preceding 2 weeks increased up to 4 years beyond high school and then dropped to levels below those of the seniors. Although 31 percent of seniors said that most or all of their friends got drunk at least once a week, this figure had dropped to 12 percent among those aged 23 to 26.

Results of the National Household Survey, conducted by the National Institute on Drug Abuse (NIDA 1988), showed similar patterns of increase and decline. In 1985, 66 percent of young people between the ages of 18 and 21 were current drinkers; the proportion rose to 76 percent for the 22-to-25 age group and then declined to 70 percent among those aged 26 to 34. The proportion of heavy drinkers also declined after age 25.

Several other studies have examined alcohol use during the transition years between adolescence and young adulthood (Donovan et al. 1983; Temple and Fillmore 1985–1986; Grant et al. 1988). A 2-year longitudinal survey of young adults 17 to 25 years old found that three-fourths of the respondents in the initial survey were current drinkers (Grant et al. 1988). Nearly half (58 percent of the men and 33 percent of the women) were heavier drinkers who had consumed six or more drinks on at least two occasions during the preceding month. When percentages of drinkers at each consumption level were compared between the initial and followup surveys, results indicated stability both for the study population as a whole and for each sex considered separately. However, placement of these subjects in eight separate age categories from 17 to 24 revealed that this apparent stability actually masked short-term changes in subjects' drinking patterns at different ages. In this single-age context, the prevalence of both current and heavier drinking generally increased between ages 17 and 22 but declined thereafter for both sexes. This finding confirmed the patterns of increase and decrease noted in the followup of high school seniors (Johnston et al. 1988) and in the NIDA survey (NIDA 1988).

Temple and Fillmore (1985–1986), similarly investigating stability and change in drinking patterns among adolescents and young adults, surveyed a group of young men over a 15-year span from age 16 to age 31. They also found, as did Donovan et al. (1983) in an earlier study, that there was little continuity in drinking behavior from adolescence to young adulthood. Only half of the heavier drinkers at age 18 remained at that level at age 31, and 7 percent of them became abstainers. Half of the 18-year-old abstainers became moderate drinkers, one-third became heavier drinkers, and only 15 percent remained abstinent. Nearly half of the moderate drinkers became heavier drinkers; most of the other half remained at the same level, except for 4 percent who became abstainers. Most of the 31-year-olds tended to drink moderately. Although Temple and Fillmore (1985–1986) detected very little stability in drinking behavior over time, Windle (1988) reinterpreted the same data and concluded that there were elements of stability as well as change across the 15-year span.

A comparison of patterns of heavy drinking among young Canadian men and women between ages 15 and 29 used different amounts of alcohol to define heavy drinking for the two sexes (Whitehead and Layne 1987). The consumption level that defined heavy drinking for females was 25 percent lower than the level used for males, in order to take into account the difference in average body weight and thus in blood alcohol concentration (BAC). With this adjustment, patterns of heavy drinking in young women were found to be very similar to patterns for young men within 4-year age groups, although rates of abstinence were consistently higher for the women. Findings of this study suggested that there may be a close similarity in patterns of heavy consumption when body weight is controlled across a variety of other demographic variables, including age, sex, employment status, and marital status. Very few studies have considered body weight differences when comparing male and female drinking patterns, and it is therefore possible that male-female differences may often be overestimated and similarities underestimated.

Older Adults

Research has consistently shown that among persons in their sixties and older, alcohol consumption levels are lower and alcohol abuse is less prevalent than in the younger age groups. However, much of this research is based on cross-sectional studies that compare different age groups at a given point in time. Longitudinal studies that track individuals over a span of several years show that consumption patterns do not change substantially over time but instead tend to remain stable as a person ages (Glynn et al. 1984; NIAAA 1988a; Stall 1986a,b). These findings suggest the possibility that the differences noted in cross-sectional studies may be cohort effects reflecting the prevailing historical and cultural influences for each generation (Dufour et al. in press; Glynn et al. 1984; NIAAA 1988a; Stinson et al. 1989). For example, a person who grew up during Prohibition would be likely to drink less than one who grew up in a later, more permissive social environment. However, Fillmore (1987a,b) tested this hypothesis in longitudinal and cohort analyses and concluded that increases in the percentage of abstainers in the older age groups were a function of age and were not historical effects. Further studies will be needed to clarify this question.

Although longitudinal studies showed that consumption remained relatively stable, when changes in consumption did occur they were more often decreases than increases (Glynn et al. 1984; Stall 1986a,b). Stall (1986a,b) found that nearly two-thirds of older male drinkers remained stable in both frequency and quantity of alcohol intake over a 19-year period, but those who did change quantity levels were more than twice as likely to decrease as to increase their consumption.

Some reasons that have been proposed for decreases in consumption by older persons include chronic health problems, with associated fear of medication-alcohol interactions; decreased income; increased sensitivity to the effects of alcohol due partly to decreases in lean body mass and hence in body water content, resulting in higher BACs for a given quantity of alcohol; changes in lifestyle associated with retirement; and the influence of drinking patterns within individuals' social networks (Glynn et al. 1984; Stall 1986a,b, 1987; Stinson et al. 1989). Early mortality of long-term alcohol abusers could be another explanation for apparent decreased consumption levels in older age groups.

Although the overall prevalence of drinking problems is lower in the later years, a phenomenon that has received little research attention is that of late-onset heavy drinking and alcoholism (Atkinson 1988; NIAAA 1988a; Stall 1986a,b, 1987). Most older individuals with drinking problems begin to abuse alcohol earlier in life and carry their problems through middle age. However, the risk for new cases, although small, continues through the later years even as overall prevalence declines. A review by Atkinson (1988) suggested that late-onset heavy drinking may begin in response to stressful life experiences such as bereavement, poor health, economic changes, or retirement, and appears to be more frequent among persons of higher socioeconomic status.

The criteria used to measure alcohol abuse have been standardized for the younger population and, in many cases, may be inappropriate for older persons. Graham (1986) analyzed five measures of alcohol abuse with respect to their applicability to older adults: level of consumption, alcohol-related social and legal problems, alcohol-related health problems, symptoms of drunkenness or dependence, and self-recognition of problems.

The first measure, self-report of alcohol consumption, is the major source of information on rates of heavy drinking. However, older persons may have difficulty with mental arithmetic and may take prescription medicines that adversely affect recent memory. Because of generational differences in perceived social acceptability of drinking by older persons, they may be more reluctant than younger drinkers to admit to their true level of consumption and thus may have a higher rate of denial of alcohol abuse. Social, legal, and health problems may include interpersonal problems, employment problems, legal or financial difficulties, drinking and driving, and neglecting responsibilities. However, an older person who is retired, does not own a car, has few family or social contacts, and has few responsibilities would not have a high score on these measures regardless of the amount of alcohol consumed. Alcohol-related illness may be difficult to separate from other chronic illness and from side effects of medication. More appropriate indicators of possible alcohol problems among older persons might include housing problems, falls or accidents, poor nutrition, inadequate self-care, lack of physical exercise, and social isolation.

For a diagnosis of alcohol dependence, the subject must be willing and able to report relevant symptoms. Inaccurate self-reports, combined with confounding symptoms of other conditions or with the effects of prescription medicines, could be major problems in arriving at a diagnosis of dependence. Graham (1986) documented a very low level of self-recognition of alcohol problems in older persons who had been admitted to treatment programs. These persons may deny that they have problems, may not recognize symptoms of alcohol abuse, or may wrongly interpret alcohol-related symptoms as aging effects.

An analysis of hospital discharge data by age group showed that from 1979 to 1985 the 65-and-older age group consistently had the highest proportion (approximately 60 percent) of alcohol-related diagnoses that were not primary diagnoses (Stinson et al. 1989). In other words, more alcohol-related morbidity was found in older patients than in the younger age groups after they had been hospitalized for other, non-alcohol-related reasons. These findings suggest that considerable alcohol-related morbidity in the older population may go undetected and untreated, and that clinicians should be alert to the possibility that some health problems in older patients may be alcohol related.

Eleven percent of the U.S. population is currently over age 60; by the year 2030, that figure will have increased to 25 percent. This increase, with associated increases in numbers of older alcohol abusers, will have serious implications for future health care providers. Recognizing the need for increased attention to the health problems of the rapidly expanding older population, the Surgeon General's Workshop on Health Promotion and Aging (USDHHS 1988) proposed a comprehensive agenda for future programs and research efforts. In the field of alcohol epidemiology, these recommendations included expanding cross-sectional and longitudinal studies and reexamining existing data sets; analyzing drinking patterns among older age groups with special attention to different socioeconomic groups, minority groups, and women; determining the extent of lifetime heavy drinking versus late-onset heavy drinking; investigating the effects of retirement, bereavement, and changes in income on alcohol consumption patterns; and further examining the reasons for decreases in alcohol consumption with increasing age.

The Homeless

Although the prevalence of homelessness is difficult to assess, it has been estimated that at least 250,000 Americans are homeless on any given night and that as many as 3 million may experience some type of homelessness each year (Ropers and Boyer 1987). Estimates of the prevalence of current alcohol abuse or dependence among the homeless generally range from 20 to 45 percent (Mulkern and Spence 1984; Wright et al. 1987), and estimates of lifetime prevalence range as high as 63 percent (Fischer and Breakey 1987; Koegel and Burnam 1987; Ropers and Boyer 1987).

The incidence of alcohol abuse and dependence among the homeless appears to be highest in the middle years, and it is substantially lower among both the young and the old (Fischer and Breakey 1987; Wright et al. 1987). In contrast, alcohol abuse and dependence in the general population is highest among the young and declines in middle age. The high prevalence of midlife alcohol abuse and dependence among the homeless lends some support to the thesis that many of these people continue to drink heavily as a means of coping with the physical and emotional stresses associated with homelessness. However, it is probably also true that alcoholism in itself puts middle-aged alcoholics at relatively high risk for becoming homeless. Low levels of alcohol abuse and dependence among the older age groups could reflect a higher mortality rate among older homeless alcoholics.

The homeless comprise a population at high risk for health problems in general, and this risk is increased by alcohol abuse and dependence. In a Los Angeles study, 57 percent of homeless alcohol abusers reported chronic health problems, compared with 43 percent of homeless nonabusers (Ropers and Boyer 1987). An analysis of health problems among 30,000 homeless clients of the privately funded national Health Care for the Homeless (HCH) program indicated that about 45 percent of men and 15 percent of women seeking health care were alcohol abusers or alcohol-dependent individuals (Wright et al. 1987).

Table 4 summarizes data on health problems diagnosed in HCH clients who were seen more than once and indicates the percentage of those with each diagnosis who were alcohol abusers. The table illustrates the range of health problems among the homeless in general and highlights the extent to which alcohol abuse may exacerbate nearly all of these problems. Figures in the ratio column indicate the degree to which alcohol abusers exceeded nonabusers in incidence of a given diagnosis. For example, the abuser/nonabuser ratio of 1.8 for hypertension among males means that male alcohol abusers were 1.8 times more likely than nonabusers to have that diagnosis. As would be expected, liver disease and drug abuse were significantly more prevalent among both male and female homeless alcohol abusers than among nonabusers.

The co-occurrence of alcohol abuse with drug abuse and mental illness among the homeless is particularly significant. In the HCH study, more than one-fourth of alcohol-abusing women and nearly one-fifth of the men abused other drugs in addition to alcohol (Wright et al. 1987). Mental illness was diagnosed in more than half of female abusers and in one-fourth of male abusers.

A study of homeless persons in Los Angeles also documented high rates of mental illness among alcohol abusers (Koegel and Burnam 1987). This study found that 69 percent of those with a lifetime prevalence of alcohol abuse or dependence had at least one non-alcohol-related psychiatric diagnosis, and that multiple psychiatric diagnoses were more likely to occur in those with alcohol problems. More than 22 percent of homeless persons with alcohol problems had three or more such diagnoses, compared with only 6 percent of those without problems. The differences were significant for diagnoses of drug abuse or antisocial personality. The alcohol abusers were also somewhat more likely to be diagnosed with affective disorders, schizophrenia, generalized anxiety, and panic disorder.

The homeless alcoholics who did not have additional psychiatric diagnoses were all male and, compared with those who had both alcohol and psychiatric problems, were much more likely to be middle aged; to be either separated, divorced, or widowed; to have children; and to be veterans (Koegel and Burnam 1987). In contrast, the homeless with both alcohol and psychiatric problems included women, were predominantly under age 40, were less likely to have been married, and included a higher proportion of blacks.

The homeless who had neither alcohol nor psychiatric problems were far more likely to be newly homeless than were those with alcohol problems, and they were far less likely to have experienced long-term homelessness (Koegel and Burnam 1987). Most of those with neither alcohol nor psychiatric problems cited loss or lack of a job as the primary reason for their homelessness. Those with alcohol and/or psychiatric problems were much more likely to cite lack of money, family crises, or alcohol problems as the cause of their homeless condition. These findings suggest that, in addition to housing and job opportunities, efforts to alleviate the problem of the large numbers of homeless persons in the United States must involve increased availability of alcoholism treatment facilities along with adequate health and mental health care.

Racial and Ethnic Minorities

Of the four major racial and ethnic minority groups in the United States, blacks are the largest, comprising 12 percent of the total population. Approximately 7 percent of the total population are Hispanics, and approximately 2 percent are Asian-Americans. American Indians and Alaska Natives are the smallest racial minority, comprising less than 1 percent of the total population.

TABLE 4. Health problems diagnosed among homeless health care clients, by sex, with percentage of alcohol abusers and nonabusers and abuser/nonabuser ratio for each diagnosis

	Men			Women		
Diagnosis	Abusers (percent)	Nonabusers (percent)	Abuser/ nonabuser ratio	Abusers (percent)	Nonabusers (percent)	Abuser/ nonabuser ratio
Mental illness	27.7	21.3	1.3	52.8	35.2	1.5
Peripheral vascular disorder	15.5	13.2	1.2	14.1	10.7	1.3
Hypertension	21.9	12.3	1.8	14.1	10.3	1.4
Gastrointestinal disorder	17.1	11.2	1.5	20.0	14.9	1.3
Trauma						
Lacerations	13.5	8.8	1.5	8.5	3.7	2.3
Fractures	7.0	4.5	1.6	5.4	2.1	2.6
Contusions	8.0	4.4	1.8	10.6	4.5	2.4
Drug abuse	18.1	7.3	2.5	26.1	5.3	4.0
Eye disorder	18.1	7.3	2.5	9.6	6.9	1.4
Neurological disorder	9.7	6.7	1.4	11.7	9.6	1.2
Cardiac disease	8.5	6.1	1.4	6.3	5.6	1.1
Tuberculosis	6.9	5.5	1.3	3.1	2.7	1.1
Chronic obstructive pulmonary disease	6.0	4.2	1.4	8.9	3.7	2.4
Arterial disease	5.4	3.5	1.5	6.8	4.0	1.7
Diabetes mellitus	2.2	2.2	1.0	3.1	2.8	1.1
Seizures	6.8	2.2	3.1	5.6	2.5	2.2
Anemia	2.2	1.4	1.6	3.1	3.6	0.9
Nutritional disorder	2.4	1.3	1.8	4.5	2.1	2.1
Liver disease	3.0	0.7	4.3	4.2	0.6	7.0
Pregnancy				7.0	12.0	0.6

SOURCE: Wright et al. 1987.

Despite considerable diversity within these groups in drinking patterns and problems, U.S. racial and ethnic minority groups have collective patterns of alcohol use and alcohol-related problems that may be quite different from those of the population as a whole. However, Lex (1987) outlined several caveats for examining these differences, pointing out that few studies of alcohol problems have involved systematic comparisons across ethnic minority groups or examined a sufficient number of relevant variables. These variables may include nutritional or health status, socioeconomic status, education, employment status, income, and housing conditions. Societal conditions, local customs, and shared beliefs about alcohol's symbolic role in a group's social life are also relevant factors.

Alcohol research has only recently begun to focus on racial and ethnic minorities. In the absence of adequate longitudinal studies, few conclusions can be drawn concerning trends in consumption patterns or problem rates. Further research is needed, both to characterize the problems that may be specific to each group and to provide a basis for culturally appropriate means of addressing these problems.

Blacks

A survey conducted in 1984 focused on obtaining representative national samples of blacks and Hispanics—the first national survey to do so (Caetano 1989; Herd 1988b, 1989). Overall, black and white men had similar drinking patterns, although black men had somewhat higher abstention rates than whites (29 percent versus 23 percent) and white men were somewhat more likely to be heavier drinkers. The same pattern was found for women, but the differences were more pronounced. Nearly half of black women were found to be abstainers (46 percent), compared with one-third (34 percent) of white women. A larger proportion of white women were heavy drinkers, although when abstainers were excluded from the analysis, a somewhat higher proportion of black female drinkers were found to drink heavily. The 1985 National Health Interview Survey, however, showed higher rates of abstention and lower rates of drinking at all levels for black men and women than for whites (NIDA 1988; Schoenborn 1986; Williams et al. 1986).

The 1984 survey found important racial differences within age-group categories. Heavy drinking was most prevalent among white men in the 18-to-29 age category and declined in successive age groups (Herd 1989). In contrast, abstention rates were high among black men between 18 and 29, but rates of heavy drinking rose sharply among those in their thirties. Similarly, young white women in the 18-to-29 age group were significantly more likely to drink, and to drink heavily, than were young black women. Other studies also have shown high rates of abstention for black adolescents and young adults (Barnes and Welte 1986; Harford 1986; Welte and Barnes 1987).

Although overall drinking levels were lower among blacks than among whites, black males surveyed in the 1984 study reported higher rates of drinking-related problems (medical, personal, and social) than white males (Herd 1989). The most striking differences between blacks and whites were in rates for health problems and symptoms of dependence. The only problem reported more often by whites than blacks was drinking and driving; more than 2.5 times more white men than black men reported driving while drunk. The overall pattern was reversed among women, with black women reporting fewer alcohol-related problems than white women, except for a somewhat higher proportion experiencing health problems. As with men, the greatest difference was in the rate of drunk driving; more than five times more white women than black women reported driving while drunk. Although arrest rates for drunk driving have been higher among blacks than among whites, the rates for whites increased significantly through the 1970s and by 1982 arrest rates were nearly identical for both groups.

Black and white men had strikingly different patterns in the relationship between age and drinking problems (Herd 1989). White men were shown to be at the highest risk for alcohol use problems in the youngest age group (18 to 29), but black men were at the lowest risk in this age group. For men in their thirties, problem rates decreased sharply for whites but increased sharply for blacks. Problem rates remained higher for blacks than for whites throughout middle and old age.

Blacks, especially males, are at extremely high risk for acute and chronic alcohol-related diseases such as cirrhosis, alcoholic fatty liver, hepatitis, heart disease, and cancers of the mouth, larynx, tongue, esophagus, and lung, as well as for unintentional injuries and homicide (Herd 1989; Ronan 1986–1987). Between 1979 and 1981 the incidence of esophageal cancer for black males aged 35 to 44 was 10 times that for whites. Although cirrhosis deaths have declined since 1973, they are still disproportionately high among blacks. Further, increased susceptibility of blacks to the deleterious effects of prenatal alcohol exposure has been demonstrated in epidemiological studies (Chavez et al. 1988; Iosub et al. 1985).

One possible explanation for the high level of health problems among blacks may be the later onset of heavy drinking (Herd 1989). This late onset may be associated with more sustained patterns of high consumption, in contrast to patterns among whites, for whom heavy drinking is more likely to be a short-term, youthful phenomenon.

Herd (1988a) examined the effect of socioeconomic factors on problem rates and found that these factors were more strongly related to drinking problems among black men than among white men. Poor education, poverty, and heavy consumption patterns were associated with both dependence problems and interpersonal problems among blacks. In contrast, only consumption patterns—but not education or income—were found to be statistically related to these types of problems among whites.

In sum, although alcohol consumption levels are very similar for black and white men, black men experience considerably higher rates of all kinds of social and health complications than white men, and high problem rates are concentrated among the more socioeconomically disadvantaged men. These findings suggest that the higher vulnerability of blacks to alcohol problems compared with whites at the same consumption level may be largely a reflection of social and economic problems such as unemployment, adverse living conditions, poor health care, and racial discrimination (Herd 1987, 1988a). The question of possible differences in biological vulnerability to some alcohol-related health problems among blacks remains unanswered; further research is needed to address this important concern.

Hispanics

Hispanics display great cultural diversity, with associated diversity in patterns of alcohol use. Although there has been considerable debate over an acceptable definition of Hispanic ethnicity (Caetano 1986a), U.S. Hispanics generally have origins in Mexico, Puerto Rico, Cuba, and other Latin American countries.

The differences in drinking norms among Spanish-speaking cultures were illustrated dramatically in an international comparison of drinking patterns among U.S. Hispanics, Mexicans in Mexico, and Spaniards in Spain (Caetano 1988b). More than half the men in Spain drank nearly every day, 5 times more than U.S. Hispanic men and 15 times more than Mexican men. Very few Spanish men were abstainers; five times more U.S. Hispanics and six times more Mexicans abstained. There were 3 times more abstainers among U.S. Hispanic women, and 4 times more among women in Mexico, than among Spanish women; 25 times more Spanish women drank nearly every day than did U.S. Hispanic or Mexican women. The low rates of abstention and high rates of daily drinking among Spanish men and women are best explained as being reflective of the drinking patterns typical of wine-drinking cultures.

A representative national sample of Hispanics in 1984 revealed striking differences in alcohol consumption between Hispanic men and women (Caetano 1989). More than 70 percent of Hispanic women drank either less than once a month or not at all; in contrast, almost the same percentage of men were drinkers. As with black men, rates of heavier drinking increased sharply among Hispanic men in their thirties but declined thereafter. Among women, rates of heavier drinking were very low except for a significant increase among women in their forties and fifties, but the rate dropped to zero among women aged 60 or over. Mexican-American men and women had much higher rates of both abstention and heavier drinking than men and women of Puerto Rican or Cuban origin.

Acculturation (the degree to which one has adapted to and accepted the social and cultural norms of a new environment) may be associated with substantial changes in drinking patterns. Caetano (1987a,b) found that the more highly acculturated men were more likely to be drinkers and to drink heavily, and that their drinking patterns were closer to those of the U.S. general population. The relationship was similar but more pronounced among women. Only half as many highly acculturated women were abstainers, and nine times more were in the two heaviest drinking categories compared with those at low acculturation levels.

A study of patterns of alcohol use by immigrant Mexican-American women found that the proportion of abstainers was considerably higher among the immigrants than among women in Mexico, in direct contrast to the pattern of increased alcohol use by immigrant Mexican men (Gilbert 1987). The immigrant women had adopted a unique pattern of consumption unlike the drinking patterns of women in Mexico, women in other Hispanic immigrant groups, and women in the U.S. general population. By the second generation, however, rates of both abstention and heavier drinking were similar to those for women in the U.S. general population.

About 18 percent of Hispanic men and 6 percent of women experienced at least one alcohol-related problem during the year preceding the 1984 survey (Caetano 1989). Problem rates varied by national origin; much higher proportions of Mexican-American men and women reported drinking-related problems, compared with Puerto Ricans and Cubans (Caetano 1988a). Among Hispanic male age groups, problem rates remained high from the twenties through the thirties whereas in the general population, problem rates dropped substantially among those in their thirties.

The prevalence of alcohol-related problems is higher among Hispanic men than among black or white men (Caetano 1986b). This high problem rate suggests a need for studies of Hispanic male adolescents to identify possible risk factors and vulnerabilities. Although a few studies have compared consumption levels in different adolescent ethnic groups (Barnes and Welte 1986; Welte and Barnes 1987), little systematic information is available on alcohol-related risk factors or patterns of drinking behavior among Hispanic male adolescents. A comprehensive literature review by Gilbert and Alcocer (1988) provides a basis for future research efforts aimed at further investigating the alcohol-related behavior of at-risk Hispanic adolescents.

Asian-Americans

The term "Asian-American" encompasses an extremely diverse population with origins in Japan, China, Korea, India, the Philippines, Vietnam, and other Asian countries. As would be expected, Asian-Americans from such disparate cultural backgrounds vary significantly in their patterns of alcohol consumption. Nevertheless, Asian-Americans as a whole have the lowest level of alcohol consumption and alcohol-related problems of all the major racial and ethnic groups in the United States (Sue 1987). This low rate of alcohol consumption and abuse may be attributed partly to cultural factors and partly to the flushing response, which occurs in a high proportion of Asian people. This physiological reaction is characterized by facial flushing, which is often accompanied by headaches, dizziness, rapid heart rate, itching, or other symptoms of discomfort.

A study carried out in California compared drinking patterns among Asian-Americans of Chinese, Japanese, Korean, and Filipino origin (Kitano and Chi 1986–1987). Rates of abstention were very high among Korean men, nearly half of whom were abstainers. Approximately one-third of Chinese, Japanese, and Filipino men were abstainers. Four-fifths of Korean and Filipino women were abstainers, as were two-thirds of Chinese women but only one-third of Japanese women. A study of older Chinese-Americans in Chicago showed that lifetime abstention decreased with advancing age (Yu and Liu 1986–1987). Abstention rates remained fairly constant at about 57 percent for those between the ages of 50 and 79, but only 45 percent of those aged 80 or older abstained. This finding suggests that many Chinese may begin drinking in old age. A possible explanation is the social acceptance of moderate drinking, ostensibly for health reasons, among elderly Chinese.

In the California study, Japanese, Korean, and Filipino men all had approximately the same percentage of heavy drinkers (about 28 percent), but only half as many Chinese men drank heavily. Twelve percent of Japanese women drank heavily, but only 4 percent of Filipino women and virtually none of the Chinese or Korean women were heavy drinkers. Lubben et al. (1988) found the same proportions of heavy drinkers among Filipino-Americans.

Despite the prevalence of heavy drinking among males in some groups, there is very little evidence of alcohol-related problems among Asian-Americans. One possible explanation is that much of the drinking appears to be done with friends and on special occasions; thus drinking behavior is socially controlled, and the result is low prevalence of alcohol-related social and personal problems. Cirrhosis mortality rates were found to be nine times higher for blacks and four times higher for whites than for Chinese-Americans, which was not unexpected, considering the substantially lower rates of heavy drinking among Chinese-Americans (Yu and Liu 1986–1987).

A cross-cultural study involving international collaboration between researchers in Japan and the United States compared alcohol consumption patterns and problems among Japanese in Japan, Japanese-Americans in California and Hawaii, and Caucasians in California (Clark and Hesselbrock 1988; Kitano et al. 1988; Towle 1988). Japanese men in Japan had the highest proportion of current drinkers and the highest consumption levels among the four groups (Clark and Hesselbrock 1988). Japanese women, on the other hand, had the lowest proportion of drinkers, and Caucasian women, the highest. Japanese men in Japan also had the highest rate of alcohol-related problems, and Japanese-Americans reported the fewest problems. The effects of acculturation on drinking patterns were not clear; results indicated that drinking patterns in all groups were highly dependent on local social and environmental influences (Kitano et al. 1988).

Sue (1987), reviewing the relatively sparse literature on alcohol use among Asian-Americans, concluded that although Asian-Americans are more likely to be abstainers than other racial groups, the frequency and amount of drinking appear to be increasing. This review stressed the importance of such variables as specific ethnic group, place of birth, generational status, and degree of acculturation in analyzing patterns of alcohol use among Asian-Americans.

American Indians and Alaska Natives

Because of the great diversity in drinking practices among American Indian tribal groups, it is not possible to make generalizations about their drinking patterns. Some tribes are mostly abstinent, while others have high levels of alcohol use and abuse. A comparative study of 11 tribal groups in Oklahoma found a wide range in percentages of deaths that were alcohol related, from less than 1 percent to 24 percent (Christian et al. 1989).

The extent of alcohol-related problems among American Indians and Alaska Natives is reflected in their mortality rates for causes that are, or are very likely to be, alcohol related. Unintentional injuries (accidents), chronic liver disease and cirrhosis, homicide, and suicide are among the 10 leading causes of death for American Indians and Alaska Natives (IHS 1988). The age-adjusted death rate for unintentional injuries, the second-ranked cause of death, dropped from a high of 184 deaths per 100,000 population in 1955 to 77.7 in 1985, a 58-percent decrease. However, this rate is still 2.2 times higher than the rate for unintentional injuries in the general population. The respective mortality rates among Indians and Alaska Natives for homicide and suicide were 14.3 and 14.1 deaths per 100,000 in 1985, compared with rates of 8.3 and 11.5 in the general population. An estimated 75 percent of all traumatic deaths and suicides among Indians and Alaska Natives are alcohol related (Rhoades et al. 1987). In Oklahoma, more than 9 percent of deaths among Indians were classified as alcohol related, compared with 2 percent for whites and 3 percent for blacks (Christian et al. 1989).

Deaths from alcohol-related causes are particularly prevalent among American Indians and Alaska Natives between the ages of 25 and 44 (IHS 1988). In this age group, the 1985 mortality rate for unintentional injuries was three times higher than the rate for the United States as a whole, and the death rate for cirrhosis was more than five times higher than for the general population.

The 1985 age-adjusted mortality rate for chronic liver disease and cirrhosis among American Indians and Alaska Natives was 29.2 deaths per 100,000, three times the U.S. death rate of 9.7 per 100,000 (IHS 1988). Deaths attributed to alcoholism in the IHS report included those caused by alcohol dependence syndrome, alcoholic psychoses, and alcohol-related liver cirrhosis. The 1985 age-adjusted alcoholism mortality rate was 26.1 deaths per 100,000 population, a significant decrease from the 1973 high of 66.1 but still four times higher than the rate for the general population. Alcoholism death rates were twice as high for men as for women and, among age groups, ranged as high as 96.8 deaths per 100,000 for men between the ages of 45 and 54.

Binge drinking is characteristic of many Indian tribal groups. This heavy, sporadic alcohol consumption may be the reason for the high rate of accidental deaths and homicides among American Indians. Male Indians living in urban areas are less likely to be involved in binge drinking, but they continue to drink heavily (Weibel-Orlando 1986–1987).

Although American Indian women drink considerably less than men, they appear to be particularly susceptible to alcohol-related health problems. For example, despite their relatively low consumption levels, women account for nearly half of cirrhosis deaths of American Indian and Alaska Natives (IHS 1988). Problems related to prenatal alcohol exposure are discussed in chapter VI.

Summary

Per capita alcohol consumption has been slowly but steadily declining in the United States since 1981. In 1987, after 6 successive years of gradual decline, per capita consumption was at its lowest level since 1970. Consumption appears to be leveling off or declining in many other industrialized countries. Nevertheless, alcohol remains the leading drug of abuse in the Nation.

Patterns of consumption remained relatively stable from the 1960s through the 1980s except for a small increase in the percentage of abstainers among men and an increase in the proportion of heavy drinkers among both men and women in their twenties. There also has been a decrease in the proportion of abstainers among younger women, but overall there is no evidence of a convergence in drinking patterns between men and women.

The prevalence of alcohol-related problems among hospitalized persons has been estimated to be 25 percent. Overall alcohol-related morbidity did not decline during the 1980s. Nearly half of those diagnosed as having alcohol abuse or alcohol dependence in the general population, and two-thirds of those in treatment for alcohol and other drug problems, have psychiatric diagnoses. Overestimation in some categories may have resulted from the diagnostic methods used in the study.

The cirrhosis mortality rate has been dropping since 1973 and in 1985 was the lowest it had been in 3 decades. There is evidence for similar declines in cirrhosis mortality in certain developed countries.

Although the level of alcohol use problems remained stable between the 1960s and the 1980s, there were small increases in the prevalence of symptoms of dependence. Both heavy drinking and drinking-related problems are associated with being male, young, and/or single. However, there is a high degree of remission of problems with increasing age, paralleling age-related decreases in heavy drinking.

Drinking-related problems among women appear to be associated with role deprivation rather than with role overload or with conflicts resulting from multiple roles. Women at highest risk for drinking-related problems are unmarried but living with a partner, are in their twenties or early thirties, and/or have a heavy-drinking husband or partner. Depression and reproductive problems may precede as well as follow heavy alcohol use.

The gradual downward trend in alcohol use by high school seniors during the 1980s continued through 1988, with declines in nearly all indicators. However, alcohol use was still disturbingly high: 92 percent of seniors in 1988 had tried alcohol, two-thirds were current drinkers, more than one-third were occasional heavy drinkers, and nearly one-third reported that most or all of their friends got drunk at least once a week. During the transition years between adolescence and young adulthood there appears to be little continuity in drinking behavior, and drinking levels tend to decline substantially by age 30.

When changes in consumption patterns occur among older adults, they are usually decreases. Thus, there are more abstainers and fewer heavy drinkers in this age group than in the younger age groups. The prevalence of drinking-related problems is lower among older people, although late-onset heavy drinking may sometimes begin in response to stressful life experiences. Alcohol-related health problems are diagnosed in a high proportion of older patients who have been hospitalized for non-alcohol-related causes.

Alcohol abuse and alcohol dependence are serious problems among the homeless: Prevalence estimates for current alcohol abuse and alcoholism range from 20 to 45 percent. The homeless are at high risk for health problems and psychiatric disorders, and these are exacerbated by alcohol abuse.

Each of the four major racial and ethnic minority groups in the United States encompasses diverse subpopulations, but each group as a whole exhibits characteristic patterns of alcohol use and abuse, and each has specific vulnerabilities. Although blacks have high rates of abstention and low rates of heavy drinking, they are at extremely high risk for health problems in which alcohol is a factor, such as liver cirrhosis, heart disease, and cancers of the esophagus, mouth, larynx, and tongue. Hispanics, particularly Mexican-Americans, have high rates of abstinence, high rates of heavy drinking, and a higher prevalence of drinking-related problems than other racial and ethnic groups. Asian-Americans have the highest rates of abstention, the lowest rates of heavy drinking, and the lowest levels of drinking-related problems, probably at least partly because of the flushing response, a physiological sensitivity to the effects of alcohol. American Indian and Alaska Native groups vary widely in alcohol use, but as a whole they have very high mortality rates from causes that are, or are likely to be, alcohol related, such as cirrhosis, unintentional injuries, homicide, and suicide.

Important areas for future epidemiologic research include continued surveillance of per capita consumption and liver cirrhosis mortality, with greater attention to international trends; standardization of measures for defining levels of alcohol consumption in order to permit greater comparability of survey data; clarification of the diagnostic distinction between alcohol abuse and alcohol dependence (and more rigorous application of this distinction in epidemiologic studies); more accurate determination of the extent of both medical and psychiatric comorbidity; more accurate assessment of the impact of alcohol abuse on mortality; and increased emphasis on longitudinal studies of drinking patterns and problems, with particular attention to understudied subgroups of the population such as older age groups, women, and racial and ethnic minorities.

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■ *Chapter III*

Genetics and Environment

Introduction

The observation that alcoholism tends to run in families has been confirmed by numerous reports in the modern scientific literature. For example, Cotton (1979), in a frequently cited review, analyzed 39 familial alcoholism studies published over a 10-year period. She found substantial agreement among the studies that an alcoholic is much more likely than a nonalcoholic to have a parent or other relative who is also alcoholic; two-thirds of the studies found that at least 25 percent of the alcoholics had alcoholic fathers. Based on her review, Cotton estimated that, on average, one-third of any sample of alcoholics will have at least one parent who is also alcoholic. Although most of the studies found high rates of alcoholism among the parents of alcoholics, several also found high rates among siblings. Fathers and brothers of alcoholics were more likely to have alcohol problems than the mothers and sisters of alcoholics, a fact that probably reflects the greater incidence of alcoholism among males. Thus many studies indicate that a major risk factor for developing alcoholism is being the close relative of an alcoholic.

As in the case of alcoholism, a number of common pathologies have been found to occur more frequently in some families than in others, including cardiovascular, neoplastic, emotional, and endocrine disorders (Williams 1988). One cannot, however, interpret such findings in exclusively genetic terms, since genetic factors in some diseases do not negate the contribution that environmental factors can make to the risk of developing such diseases (Williams 1988).

Traits that are familial may be passed from generation to generation by genetic factors or environmental factors. Research has produced evidence that both genetic and environmental factors contribute to alcoholism, and the interaction of genetic and environmental factors is emerging as a fundamentally important issue in the etiology of alcohol problems. As yet, the specific gene or genes involved have not been identified and the mechanisms by which genetic transmission occurs have yet to be defined. Likewise, the specific environmental risk factors are not known, although research does suggest possible childhood antecedents of alcoholism as well as potential psychological and social mechanisms related to drinking behavior and to the process of becoming dependent.

It is most plausible that the relative contribution of genetics or environment to the expression of alcohol problems in any given individual will vary depending on a number of factors including the subtype of alcoholism (Cloninger et al. 1981).

For example, one form of alcoholism appears to be highly dependent on genetic factors, another form appears to require both specific genetic and environmental factors, and there are also cases of alcoholism without any obvious genetic factors (Cloninger et al. 1981).

The discussion begins with a review of recent studies involving both humans and animals that collectively point to the influence of heredity in the establishment of drinking patterns and in susceptibility to alcoholism. This review is followed by a discussion of research on psychological and social factors that influence drinking behavior. The chapter includes a discussion of possible heredity-environment interactions in the development of alcoholism, an area that seems likely to receive much more attention in the future.

Twin and Adoption Studies

Numerous studies have demonstrated that alcoholism tends to run in families and that the pattern is consistent with genetically transmitted susceptibility. Other explanations, however, are possible, because the social environment shared by members of the same family could also predispose to alcoholism. For this reason, studies assessing the role of genetics in alcoholism must minimize or control for environmental variables. Several different approaches are possible, including the study of twins and adoptees. In addition, animal research permits the study of genetic transmission of alcohol-relevant traits.

Twin studies are based on the principle that if a trait (for example, alcohol dependence) has genetic determinants, then persons who are genetically identical (identical twin pairs) should tend to develop more similar drinking patterns and problems than those who are genetically no more alike than ordinary siblings (fraternal twin pairs). Adoption studies are based on the principle that children born to alcoholics but adopted at an early age and raised by others, even in a nonalcoholic environment, may have a greater tendency to abuse alcohol or become alcohol dependent if they have inherited genes that make them vulnerable.

Twin Studies

One of the earliest studies of alcoholism in twins was by Kaij (1960), who found 74 percent concordance of alcoholism between identical twins. That is, if one member of a pair of genetically identical twins was alcoholic, the probability of the other member's also being alcoholic was 74 percent. In contrast, concordance of alcoholism between fraternal twins was only 32 percent. A higher concordance rate among identical than among fraternal twins was also found by Hrubec and Omenn (1981), who reported 26-percent concordance of alcoholism in identical twins and only 13 percent in fraternal twins.

The higher concordance of alcohol dependence rates among identical twins compared to fraternal twins suggests that genetic factors are involved in predisposition to alcoholism. Identical twins have identical genetic makeup because they developed from the same fertilized ovum. Because alcohol dependence more frequently affects both members of identical twin pairs than both members of fraternal twin pairs, a plausible explanation is that it arises from shared genetic vulnerability.

An environmental explanation is also possible. For example, Partanen et al. (1966) suggested that part of the concordance of alcohol abuse patterns between twins arises from their tendency to be socially closer than nontwin siblings and, therefore, presumably more imitative. Other studies (Kaprio et al. 1979; Kaprio et al. 1978) have found that the frequency of social contact is especially high between identical twins; a study of twin brothers in the United Kingdom (Clifford et al. 1981) found evidence suggesting that at least 20 percent of the variance in alcohol consumption could be attributed to shared family experiences.

The issue of the confounding effects of social contact between twins was addressed in a recent Finnish study (Kaprio et al. 1987) of concordance of alcohol use patterns in adult twin brothers between the ages of 24 and 49. This study, involving virtually the entire population of twins in that age group in Finland (more than 2,800 pairs, nearly one-third of whom were identical twins), is the largest to date on the concordance of drinking patterns among twins.

Subjects were given a questionnaire to determine frequency and quantity of drinking, drinking "density" (regularity of drinking at particular times, such as weekends), frequency of passing out from drinking, and frequency of social contact between twins, including cohabitation. Analysis of the data showed that cohabitation or frequent social contact between twins was indeed correlated with concordance in their drinking patterns, that identical twins had more social contact with each other during adulthood than fraternal twins, and that concordance of drinking patterns was greater between identical twins. However, greater social interaction did not fully explain the strongly similar drinking habits of identical twins, and analytical methods that adjusted for the contribution of cohabitation and social contact variables revealed a significant genetic contribution to the concordance.

For measures of frequency, quantity, and density of drinking episodes, genetic factors were significant, with heritability estimates ranging from 36 percent to 40 percent (Kaprio et al. 1987). Genetics was found to play no role in the frequency of drinking to unconsciousness. The investigators concluded that the greater similarity in drinking patterns reported by identical twin brothers cannot be fully explained by their greater social contact with each other, and that genetic factors play a significant role in the similarity of their drinking patterns.

One of the most recent twin studies (Heath et al. 1989) was also quite large, obtaining drinking information from a population of more than 1,200 identical and more than 750 fraternal female twin pairs located through the Australian National Twin Register. These sample sizes were large enough to permit a detailed analysis of the interaction of genetic and environmental factors in determining alcohol consumption levels.

In addition to questions about alcohol consumption, the respondents, whose average age was about 35, were asked for information about their marital status (which turned out to be a very influential environmental variable) and the amount of social contact between twins.

Unlike the study of Finnish male twins (Kaprio et al. 1987), analysis of the Heath et al. (1989) data gave no evidence that concordance of drinking habits in these female twin pairs was influenced in any way by either their frequency of social contact with each other or by their cohabitation. This finding might reflect gender differences in social influences on drinking habits or cultural differences between Finland and Australia.

The most significant finding, however, was a significant interaction between genetics and environment in relation to marital status, which was found to be a major modifier of genetically influenced drinking habits. (For purposes of statistical analysis, living together with a man was considered the equivalent of marriage.) In the younger cohorts (age 30 and under), genetic differences accounted for 60 percent of the variance in drinking habits in twins who were not married, but for only 31 percent of the variance in married twins. Likewise, in the older cohorts (age 31 and older), genetic factors accounted for 76 to 77 percent of the variance in drinking habits in the unmarried women, but for only 46 to 59 percent of that variance in married respondents. In other words, in both cohorts, being married or having a marriagelike relationship modified the magnitude of the impact of inherited factors that affect drinking behavior.

Another recent twin study investigated factors associated with adolescent alcohol use. Heath and Martin (1988) surveyed adult twin pairs (aged 20-30) from the Australian National Twin Register concerning their current and teenage alcohol use in a study of genetic and social determinants of adolescent drinking. When genetic and shared environmental effects were pooled, the resulting measure of familial influences was substantially important in explaining age of drinking onset during adolescence, accounting for 51 percent of the variance in males and 58 percent in females. Gender differences were found to exist, however, in the relative importance of genetic and shared environmental factors. Among males, age of initiation of drinking was uninfluenced by genetic factors but strongly influenced by shared environment; among females, moderate genetic influence and little shared environmental effect were found. In contrast, current alcohol consumption among adult twins was strongly influenced in both sexes by genetic factors, which accounted for 58 percent of the variance in consumption in females and 45 percent in males, while 0 and 21 percent respectively was accounted for by shared environment.

Martin et al. (1985a) found genetic influences in psychomotor performance and pulse rate among twins following alcohol ingestion. Alcohol administered acutely to 206 twin pairs (42 percent of them identical) elicited great differences in psychomotor and psychological responses in individuals that had not been apparent during sobriety. About half the total variance in body sway immediately after alcohol ingestion was found to be due to genetic differences. Significant genetic contributions were also found in the variance of alcohol-elicited effects on hand steadiness, arithmetic ability, and pulse rate. These variations were significantly correlated with measures of blood alcohol concentration (BAC), previous drinking experience, and extraversion in the subjects. However, analysis led to the conclusion that very little of the genetic variation could be explained by these correlated factors, and that most of it was due to genetic factors.

Adoption Studies

The *Sixth Special Report to the U.S. Congress on Alcohol and Health* (USDHHS 1987) gave considerable attention to adoption studies which had shown that children born to alcoholic parents but adopted during infancy and raised by others were at greater risk for alcoholism than adopted children who were born to nonalcoholics (Cloninger et al. 1981; Goodwin et al. 1973).

Adoption studies are important because they allow genetic and environmental factors to be assessed independently. Thus the effects of environmental factors can be estimated by comparing individuals with different genetic backgrounds who were raised in the same home (adoptees and their nongenetic siblings), and genetic influences can be assessed by comparing genetically related individuals who were raised in different environments (adoptees and their nonadopted genetic siblings).

The *Sixth Special Report* summarized adoption studies conducted in Sweden (Bohman et al. 1981; Cloninger et al. 1981). These studies, which examined the backgrounds of both adoptive and biological parents in relation to the existence and extent of alcohol abuse and alcohol dependence in the adopted offspring, led to the recognition of two types of alcoholism having different patterns of inheritance: type 1, milieu-limited; and type 2, male-limited. (These typologies are discussed more fully later in this chapter.) As with earlier studies in Denmark by Goodwin et al. (1973), the Swedish studies found no correlation of alcohol dependence between adoptive parents and adoptees.

It must be noted that some authors have found previous twin and adoption studies unconvincing (Peele 1986; Murray et al. 1983; Fillmore 1988a,b; Searles 1988). Criticisms involve possible biases introduced by adoption agency practices that match adoptees and adoptive parents and by the effects of use of subject cohorts spanning several decades. In addition, generalizability concerns were expressed based on both the use of nonstandard definitions of alcoholism and on possible differences between persons who place their children for adoption and persons who do not. Whether procedural imperfections in twin and adoption studies would be sufficient seriously to weaken their major conclusions is a question that can be settled only by further research.

Evidence for genetic factors in alcoholism does not rest on twin and adoption studies alone. Evidence of a genetic contribution also may be found in research into possible markers of genetic susceptibility and research with animal models that transmit alcohol-related behaviors to their offspring.

Animal Studies

The role of genetics in alcohol-related behaviors is supported by animal selective breeding studies that have produced genetic lines differing in a number of alcohol-related traits. These include alcohol-preferring (P) and alcohol-nonpreferring (NP) rats (Li et al. 1981); long-sleep and short-sleep mice that differ in sensitivity to alcohol's hypnotic effects (McClearn and Kakihana 1981); mouse lines that differ in susceptibility to alcohol withdrawal seizures (Crabbe et al. 1985); mouse lines that differ in sensitivity to alcohol-induced hypothermia (Crabbe, Kosobud, et al. 1987); and mouse lines that differ in sensitivity to alcohol-induced locomotor activation, a potential animal model of alcohol euphoria (Crabbe, Young, et al. 1987).

The P rat line meets all pharmacological criteria for an animal model of alcoholism (Cicero 1979). P rats voluntarily consume and work to acquire alcohol in amounts sufficient to cause intoxication even when water and other nutrient sources are freely available (Li et al. 1979; Lumeng and Li 1986; Murphy et al. 1986). P rats have been found to seek higher doses of alcohol by pressing a lever that delivers it even when delivery is intragastric rather than oral (Penn et al. 1978; Waller et al. 1984). Thus, it appears that P rats prefer alcohol not for its taste or smell but for its effects. Because of their propensity to self-administer alcohol continuously, P rats develop tolerance to alcohol, both metabolic (Lumeng and Li 1986) and neuronal (Gatto et al. 1987a,b), as well as physical dependence (Waller et al. 1982).

Continuing research on P and NP rats has revealed further contrasts between these lines. When the blood alcohol concentration (BAC) in P rats reaches 40 to 75 mg/dL, their physical activity level rises (Waller et al. 1986), but this stimulation is not seen in NP rats administered alcohol. The two lines also differ in electroencephalograph (EEG) patterns at this level of alcohol exposure (Morzorati et al. 1988). Furthermore, low to moderate doses of alcohol are reinforcing to P rats but not to NP rats, and it takes more alcohol to produce aversion in P rats (Froehlich et al. 1988). Moderate to high doses of alcohol produce impairment in both lines in a shock-avoidance task, but the impairment diminishes more rapidly during the experimental session in P rats because of more rapid tolerance development (Waller et al. 1983). Recently, it has been shown that alcohol tolerance develops more rapidly and persists much longer in P rats than in NP rats (Gatto et al. 1987a,b).

EEG differences have been found by Morzorati et al. (1988) in brain cortical and hippocampal areas in P and NP rats in response to *low alcohol* doses. Alcohol produced a persistent increase in EEG power (indicating decreased arousal) in cortical and hippocampal brain areas of NP rats. In contrast, the P rats showed an initial decrease in EEG power, then a return to baseline. Because a decrease in EEG power indicates a more aroused state, the results suggest that the P rats were mildly stimulated by the low alcohol dose while the NP rats were mildly sedated. The findings are consistent with earlier research (Waller et al. 1986) that found increased spontaneous locomotor activity in response to low doses of alcohol in P rats but not in NP rats.

Neurochemical differences also have been found in the brains of P and NP rats. The differences appear to be inborn because they are found even when the animals never have been exposed to alcohol. A consistent major difference is reduced levels of the neurotransmitters serotonin and dopamine and their derivatives in several brain regions in P rats (Murphy et al. 1982, 1987). Evidence from pharmacologic studies indicates that alcohol preference or nonpreference in the two rat lines may be related to these neurochemical differences. For example, administration of fluoxetine, which raises brain serotonin levels in the synapse by preventing its reuptake by nerve cells, and GBR-12909, which raises brain dopamine levels by the same mechanism, have been found to reduce alcohol consumption in P rats (Murphy et al. 1985; Murphy et al. 1988).

Alcohol consumption by P rats was also reduced by trifluoromethylphenylpiperazine (TFMPP) (Murphy et al. 1988). Because TFMPP is an agonist (a naturally or synthetically produced agent that mimics the activity of another substance) for a class of serotonin receptors, the finding further supports the involvement of serotonin and its receptors in alcohol preference (Murphy et al. 1988). Recent neuropharmacological studies suggest that drugs that act upon other neuroreceptor systems, such as endogenous opioids (e.g., naloxone) and gamma-aminobutyric acid (e.g., Ro15-4513), are also effective in suppressing voluntary drinking in P rats (Froehlich et al. 1988; McBride et al. 1988).

Significant findings relevant to the genetics of alcohol dependence have also come from studies of inbred mouse lines differing in alcohol preference or nonpreference. A recent study (D. Goldman et al. 1987) found evidence that variation in a single identified gene is associated with increased alcohol consumption levels in preferring and nonpreferring inbred mouse strains. The gene, found on mouse chromosome 1, is responsible for the synthesis of a protein called LTW-4, which is abundant in the brain, liver, and kidneys of these animals. A correlation was found between the possession of a variant of this gene and preference for alcohol. The correlation may indicate that alcohol preference arises directly from the properties of this gene and its product; on the other hand, it may indicate that alcohol preference arises from the properties of a nearby gene that is closely linked to the LTW-4 gene. A similar association between the possession of a variant brain protein has been suggested in human alcoholics. It has been reported that a specific variant of the human brain protein PC-1 Duarte has an increased frequency in populations of alcoholics, as well as in populations of persons with multiple sclerosis and depression (Comings 1977); PC-1 Duarte, however, differs from LTW-4 and their respective functions are unknown. There is also an indication that Protein III, a protein that plays a critical role in the functioning of nerve cells, may exist in a genetically defined variant form in individuals at heightened risk for alcohol dependence (Perdahl et al. 1984).

Although animal studies show that alcohol consumption can be markedly altered by genetic selection, there is recent evidence that alcohol consumption can be increased even in alcohol-nonpreferring lines by appropriate environmental manipulations. Recently, Samson et al. (in press) found that NP rats could be conditioned to self-administer considerably more alcohol than they otherwise would. The animals were initiated to alcohol by experimental arrangements that used a sugar solution as a reward for consumption of an alcohol solution and that did not require restriction of food or water. Thereafter, the conditioned animals would consume alcohol in concentrations as high as 40 percent and choose alcohol over water. Although self-administration produced BACs as high as 110 mg/dL in the NP rats, their alcohol intake never approached that of the

P rats, and their drinking patterns were different. These findings indicate that environmental manipulations can increase alcohol intake in this alcohol-nonpreferring line but the increase is limited by genetic factors.

In summary, animal lines have been studied that display not only many of the characteristics of human alcoholism but also genetic differences in brain neurochemistry that exist even in alcohol-naive animals and appear to be related to their inherited alcohol-seeking behavior. It is unlikely that a complex disorder like human alcoholism (or even alcohol preference in animals) could ever be fully explained in terms of the action of a single gene. Nevertheless, the recent evidence of a strong association between a particular gene and alcohol preference in mice is significant. The finding links the propensity of these mice to drink alcohol to the fundamental unit of inheritance in all organisms—the gene. Animal genetics studies provide additional evidence that genetic components can exist in human drinking behavior as well.

Potential Markers of Susceptibility

An important aspect of genetics research on alcohol-related behaviors is the study of potential behavioral, physiological, and biochemical markers of genetic susceptibility to alcoholism. As noted by Tabakoff and Hoffman (1988), such markers may be of two general types: factors that predispose to alcohol dependence and are directly involved in its development, and factors that are not themselves predisposing but are correlated with those that are.

Begleiter and Porjesz (1988) considered the following to be necessary criteria for the identification of a potential biological marker: (1) in the general population it must be shown that the trait is stable over time, reliably measurable, genetically transmitted, infrequent, and able to identify individuals at risk; (2) in patients it must be shown that the trait is common, persists during symptom remission, occurs among a patient's first-degree relatives at a higher frequency than in the general population, and tends to accompany the illness among relatives who have the same condition as the patient. The general approach in searching for markers of predisposition is to compare alcohol-dependent persons with nonalcoholic control subjects to see if they differ in particular measurements. If differences are found, it is always necessary to apply the appropriate criteria to establish that they are truly markers of predisposition (trait markers) and not a consequence of prolonged alcohol abuse (state markers).

Electrophysiological Markers

Several developments in biological marker research were described in the *Sixth Special Report*, including identification of certain brain electrical phenomena in persons at risk of becoming alcoholics (Porjesz and Begleiter 1979, 1985; Begleiter et al. 1984). In particular, many studies have focused on the electrical brain wave known as the P3 component or P3 wave. This brain wave normally appears during the performance of cognitive tasks. The strength of the P3 wave is measured by its amplitude (i.e., height) on an EEG. (More detailed discussion of the P3 wave appears in chapter IV.) Reduced amplitude of the P3 component of the event-related potential was found in young boys who had never drunk but were at risk of alcoholism because their fathers were alcoholic (Begleiter et al. 1984). Similar findings have been reported by other investigators (O'Connor et al. 1986, 1987; Steinhauer et al. 1987; Whipple et al. 1988).

More recent research findings in this area have been somewhat mixed. For example, Polich and Bloom (1988) reported that they were unable to replicate their own previous findings (Elmasian et al. 1982) of differences in the P3 amplitude in young men at risk for alcoholism and in control subjects. The more recent study was closely similar in design to the first but used a larger population of subjects and a longer period of exposure to the stimulus that evokes the P3 voltage. No significant differences in P3 amplitude were found between groups in the second study; experimental and control groups exhibited about the same decrease in P3 amplitude in response to a stimulus.

Polich and Bloom (1988) tentatively attributed the positive findings of their first study and the negative findings of their second to sampling error caused by the smaller subject groups in the first study. However, it is conceivable that the use of college students as subjects in this research also might have introduced problems. For example, it is difficult to assess the presence or severity of alcoholism in the fathers of college students since they usually are not accessible to investigators. It also is possible that, since the research employed a college population, the children of some alcoholic subtypes (e.g., type 2) may be significantly underrepresented. Despite some inconsistent findings across various studies, the investigation of the P3 wave and other brain electrical phenomena as potential markers of risk for alcoholism continues to be an active area of research.

In a recent study, Porjesz et al. (1987) replicated their previous findings of reduced P3 amplitudes in which abstinent alcoholics were presented with a task requiring them to discriminate a single designated visual stimulus occurring infrequently in a series of other visual stimuli occurring frequently (Begleiter et al. 1980; Porjesz and Begleiter 1982, 1985; Porjesz et al. 1980). A difference between this study and the earlier ones was that the abstinent alcoholics were presented with more than one meaningful visual stimulus in a series of extraneous stimuli. The meaningful stimuli had equal probabilities of occurring and were task relevant and motivationally significant (because of a $1 award for timely pressing of a switch in response to the stimulus and a $1 "fine" for tardiness). Despite the incentives, the P3 waves evoked by this test had lower amplitudes in the alcoholics than in the nonalcoholic control subjects. As with the earlier P3 studies by these investigators, the results suggest multiple deficits in cortical brain areas involved in the generation of the P3 wave, particularly in motivational and cognitive systems involved in information processing.

Electrophysiological studies have also continued with alcohol-naive boys who are at risk for alcohol dependence because their fathers are alcoholic. The finding of Begleiter et al. (1984) that young boys who had never used alcohol or other drugs showed significantly reduced P3 amplitudes like those seen in abstinent alcoholics suggests that the trait precedes the development of alcoholism and might be a genetic marker of predisposition. Begleiter, Porjesz, Rawlings, and Eckardt (1987) recently extended these findings in a study of young boys whose fathers were judged to have the severe and highly heritable type 2 (male-limited) alcoholism by criteria derived from findings in the Stockholm adoption study: early onset; episodes of hospital treatment for alcoholism; high recidivism; and a high incidence of antisocial behaviors such as fighting and traffic violations leading to arrests and other encounters with the legal system.

In this study, high-risk subjects were matched with low-risk sons of nonalcoholic fathers for socioeconomic status, education, and age and, as in the previous study, none of the boys, aged 7 to 15, had ever used alcohol or other drugs. Although there were some differences in the electrophysiological procedures used in the two studies, the second yielded the same result as the first: a significantly lower P3 amplitude in the high-risk group.

In another recent study, Begleiter, Porjesz, and Bihari (1987) tested young alcohol-naive boys to see if another electrical brain wave, the auditory brainstem potential (ABP), also might differ in the sons of alcoholic and nonalcoholic men. The ABP, a voltage generated in the brainstem in response to sounds, has previously been shown to be significantly delayed in abstinent alcoholics (Begleiter et al. 1979). Although it might be assumed that this deficit is a consequence of prolonged alcohol abuse, it is conceivable that, like reduced P3 amplitude, it precedes the development of alcoholism and thus may be a marker of predisposition to it. In contrast to the P3 marker studies, however, Begleiter, Porjesz, and Bihari (1987) found no differences in ABP between the sons of alcoholics and the sons of nonalcoholics. This finding indicates that ABP deficits in alcoholics are indeed a consequence of alcoholism (e.g., a state marker).

EEG studies also have demonstrated differences between persons with and without a family history of alcoholism. Both alcoholics and their male children have been found to have excessive beta wave activity in their EEGs compared to nonalcoholics and children without a family history of alcoholism (Gabrielli et al. 1982; Pollock et al. 1983). Other studies have found similarities between twins in the way their bodies respond to alcohol. Similar EEG and other physiological responses to alcohol as well as similar alcohol metabolic patterns have been found (Propping 1977; Martin et al. 1985b; Vessel 1973). Propping (1977) for example, found that identical twins were more similar to each other in EEG responses to alcohol than were fraternal twins.

Subjective Responses to Alcohol

Subjective responses to alcohol also have been investigated as a possible genetically linked trait marker. Schuckit (1984b) found that individuals with an alcoholic first-degree relative reported diminished subjective responses to alcohol ingestion compared with controls without a family history of alcoholism. The two groups did not differ in baseline mood before they received alcohol.

The results of a recent study by Moss et al. (1989) also suggest that sons of alcoholic fathers exhibit mood patterns in the drinking situation that differ both qualitatively and quantitatively from those seen in sons of nonalcoholics whether they consume alcohol or not—that is, these differences were observed not only in response to high and low alcohol doses but also in response to a placebo beverage. High-risk subjects scored higher on measures of tension, depression, and fatigue, independent of the alcohol content of the beverage they consumed (from high dose to low dose to placebo), and they reported less perceived intoxication at all three levels of alcohol exposure.

Feelings of anger were affected very little by alcohol dose in the low-risk group, but they were strongly dose-dependent in the high-risk subjects. The sons of alcoholics scored significantly higher on measures of anger than the sons of nonalcoholics after consuming either placebo or a low alcohol drink, but a high dose of alcohol caused much more abatement of angry feelings in the high-risk group.

These findings do not necessarily point to a genetic mechanism, although they are consistent with such a mechanism. The investigators themselves considered it more likely that expectancies about alcohol played a significant role in the observed effects of alcohol on mood in their high- and low-risk subjects (Moss et al. 1989). (The importance of alcohol expectancies is discussed in more detail later in this chapter.)

Endocrinological Markers

Several investigators have reported differences in the endocrine system in persons with and without a family history of alcoholism. Plasma levels of the hormones cortisol and prolactin, which normally increase after alcohol ingestion, have been found to display different patterns of elevation in family-history-positive and family-history-negative individuals. Diminished cortisol response to alcohol ingestion has been found in men with a family history of alcoholism (Schuckit 1984a). Schuckit et al. (1983, 1987) also found that prolactin rose to similar levels after standard doses of alcohol in male subjects with or without a family history of alcoholism, but that the levels dropped more rapidly in men with a positive family history. However, these findings were not confirmed in the study by Moss et al. (1989), who found that differences in prolactin levels between sons of alcoholic fathers and sons of nonalcoholic fathers were not statistically significant. Moss et al. (1989) suggested that the discrepancy could be due to differences in assay methods for prolactin in the two laboratories, differences in statistical methods, and differences in sample size.

Biochemical Markers

Enzyme Markers

Numerous reports have been published on the enzyme monoamine oxidase (MAO) as a potential marker of predisposition to alcoholism. MAO, which is involved in the metabolism of biogenic amines (a class of chemicals that includes neurotransmitters), exists in two forms, designated A and B. Both forms of MAO are found in the brain, but blood platelets contain only type B.

Several investigators have reported lower platelet MAO levels in alcoholics than in controls (Tabakoff et al. 1988; Faraj et al. 1987; Schuckit et al. 1982). There also is evidence that a low level of platelet MAO may be a marker of risk for a variety of psychiatric disorders in addition to alcoholism (Rice et al. 1984). Differences in platelet MAO levels between at-risk groups and control groups are not sharply demarcated, however; high individual variability in MAO levels tends to cause substantial blurring of group differences, which nevertheless have been found to be statistically significant.

Another issue is whether the generally lower level of MAO in alcoholic populations is a consequence of prolonged heavy alcohol consumption or a genetic trait that precedes the development of alcoholism. Studies in which rodents were given alcohol over an extended time period found little change in brain MAO levels (Wiberg, Wahlstrom, and Orland 1977; Tabakoff and Boggan 1974), suggesting that alcohol does not necessarily reduce MAO. On the other hand, platelet MAO levels have been shown to rise transiently in human alcoholics when they become abstinent (Major et al. 1981; Wiberg, Gottfries, and Oreland 1977). This elevation might be due to increased formation of new platelets, which are richer in MAO (Tabakoff and Hoffman 1988).

Variability of findings among MAO researchers could, in part, result from failure to take alcoholism subtypes into account (Tabakoff and Hoffman 1988). For example, research by von Knorring et al. (1985) demonstrated significant differences in MAO levels in type 1 (milieu-limited) and type 2 (male-limited) alcoholics. Subjects with the severe and highly heritable type 2 alcoholism had significantly lower platelet MAO levels than controls or type 1 subjects. More recent research from the same laboratory (von Knorring et al. 1987) showed that teenage boys who abused multiple drugs and had personality traits consistent with type 2 alcoholism also had low platelet MAO activity.

Another platelet enzyme, adenylate cyclase (AC), has recently been investigated as a possible marker of predisposition to alcoholism. This enzyme catalyzes the conversion of adenosine triphosphate to cyclic adenosine monophosphate (cAMP), a compound involved in the regulation of numerous cellular processes. Tabakoff et al. (1988) reported that baseline levels of AC were the same in the platelets of alcoholics and nonalcoholics, but that stimulation of additional activity by fluoride, guanine derivatives, and other agents was less effective in the platelets from alcoholics. This effect was not associated with smoking, race, other drug use, or duration of alcohol problems, which suggests that low responsiveness of platelet AC activity to stimulation might be a genetically influenced characteristic of alcoholic subjects. Discriminant analysis using alcohol inhibition of MAO and fluoride stimulation of AC as variables correctly classified 75 percent of alcoholics and 73 percent of controls (Tabakoff et al. 1988).

Differences in platelet AC activity also were found in a recent Swedish study comparing male alcoholics and controls (Hoffman et al. 1989). The investigators found that stimulation of platelet AC activity by guanine nucleotide and fluoride was significantly lower in the alcoholics. This effect did not appear to be caused by chronic alcohol consumption, because the effect was lowest among alcoholics who had been abstinent longest—the opposite of what could be expected if the suppression were caused by chronic alcohol ingestion. The involvement of hereditary factors is further suggested by the finding that stimulation of AC activity was lowest in the alcoholics who had the greatest number of alcoholic first-degree relatives. Similar findings were obtained in a study of Japanese alcoholics (Watanabe et al. 1988). Stimulation of platelet AC activity by alcohol was lower in alcoholics than in controls, and the differences still existed 4 weeks after withdrawal.

Serological Markers

Other proteins have been investigated as potential markers of predisposition to alcoholism. For example, the frequency of an antigen, CW3, part of a group called human leukocyte antigens (HLA), has been observed more frequently in alcoholics than in controls and even more frequently in alcoholics with liver disease (Shigeta et al. 1980). A study of 11 serological (blood) markers in alcoholics (Hill et al. 1975) found a higher frequency of particular blood group factors among alcoholics and their first-degree relatives. The chromosomal locations of the genes for these factors are known (HLA antigens are on chromosome 6 and blood group markers are on chromosome 4), and it is conceivable that future studies may link risk factors for alcoholism to specific genes.

Genetically Derived Protective Factors

Genetic research is not limited to the study of traits associated with increased susceptibility. There also is considerable scientific interest in factors that may protect against heavy drinking and thereby the development of alcohol dependence. The most notable and best studied phenomenon is the dysphoric, or flush, reaction to alcohol observed among many individuals, particularly Asians.

This phenomenon appears to relate to the presence of particular genetically defined variant forms of the enzymes of alcohol metabolism, alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH). The *Sixth Special Report* reviewed evidence that an inactive form of mitochondrial ALDH that is very common in some Asian populations may explain their lower prevalence of alcoholism (Agarwal et al. 1981; Yoshida et al. 1984; Goedde et al. 1983; Goedde and Agarwal 1987). The inactivity of the variant ALDH causes tissue acetaldehyde (ACH) levels sufficient to produce the unpleasant symptoms of the so-called alcohol flush reaction. The discomfort of this reaction may be a deterrent to drinking. Studies have shown that the frequency of the inactive ALDH is much lower among Japanese alcoholics than in the general Japanese population (Harada et al. 1982; Harada et al. 1983; Harada et al. 1985). Only 2.3 percent of Japanese alcoholics and 2.8 percent of those with alcoholic liver disease had the inactive form of ALDH, whereas the frequency of this enzyme form is 41 percent in the general population of Japan (Harada et al. 1982; Harada et al. 1983). The genetic absence of this enzyme constitutes a negative risk factor, whereas its presence is permissive of heavy drinking.

Recently, Crabb et al. (1989) reported their findings on the molecular structure of the inactive ALDH variant. Their molecular sequencing study of the enzyme from Japanese donors revealed that the inactivity of the variant form is due to a single mutation that has resulted in a substitution of the amino acid lysine for glutamic acid at position 487 of the chain of amino acids comprising the basic subunit of this enzyme.

Experiments with DNA probes (Crabb et al. 1989) confirmed previous family studies (Schwitters et al. 1982) that suggested dominance of the abnormal form over the normal form. Thus, persons who inherit the mutant gene from one parent and the normal gene from the other parent (heterozygous individuals), as well as those who inherit the mutant gene from both parents (homozygous individuals), will be deficient in this enzyme activity. Consistent with this was the finding, from the examination of white blood cell DNA, that two of the studied individuals are heterozygous for this gene (that is, they possess one gene for the inactive form and one for the active form) yet frequently experience the alcohol flush reaction.

Although evidence from twin, adoption, animal, and marker studies strongly supports the involvement of genetic factors in the development of alcohol-related behaviors and alcohol dependence, few if any scientists would argue that heredity alone can explain alcoholism. Psychological and social factors influence drinking behaviors, and the interaction of genetic and environmental factors contributes to the development of alcohol dependence.

Psychological and Social Processes

The process of becoming dependent has recently become the focus of attention in the search for psychological and social mechanisms in the development of alcoholism. Marlatt et al. (1988) observed that the psychosocial literature on addiction generally identifies three stages in its development: initiation of alcohol and other drug use; reinforcement of alcohol and drug use in the transition to escalated use, tolerance, and dependence; and attempts to overcome the addiction. The initiation, continuation, and intensification of drinking are only preconditions for the development of alcohol dependence. Relevant behavioral factors in the progression include changes in the importance of drinking in one's life and preoccupation with alcohol use. The essential features of alcoholism are tolerance (marked by diminishing responsiveness to alcohol) and dependence (manifested by signs and symptoms of physical and psychological distress when alcohol is withdrawn). Biological factors can increase the risk of becoming dependent on a drug such as alcohol, but only in the context of environmental factors that are themselves predisposing (Connors and Tarbox 1985).

A number of large studies of initiation (Chassin 1984; Long and Scherl 1984; Jessor 1986; Kaplan 1985; Sadava 1987) have identified several factors that consistently predict initiation of alcohol and drug use and dependency in young people. They include alcohol and drug use by peers or parents, delinquency, sociopathy in the parents, poor self-esteem, social nonconformity, and stressful life changes. Many intervention programs aimed at adolescents are intended to prevent the initiation to drug and alcohol use. Their success so far has been mixed (see chapter IX).

Use of alcohol is "social" during the initiation stage, and for most individuals it never goes beyond that stage. The factors responsible for transition from social drinking to greatly intensified drinking are of considerable interest to researchers, because that transition is an obvious early requirement for the eventual development of alcohol dependence. Work by several investigators (Donovan 1988; Galizio and Maisto 1985; Peele 1985; Wallace 1985; Zinberg 1984) indicates that factors likely to be involved in intensification and transition to dependence are the pharmacologic effects of alcohol; the psychological state of the user, especially expectations about alcohol's effects; and characteristics of the setting in which alcohol is used.

A major feature of alcohol and other drugs is that they initially produce pleasant effects that reinforce continued consumption (Barrett 1985; Hunt 1987a,b). Reinforcement is widely believed to play a major role in alcohol abuse and dependence. Although there is much research to be done in this area, it is known that alcohol produces reinforcement in at least two ways: by producing mild euphoria and by reducing anxiety. (Animal and human research that provides evidence for both effects is discussed in chapter IV.) The two effects probably vary from one individual to another, with one effect acting as the predominant reinforcer. It is possible that the differences in alcohol preference observed in genetic strains of rats and alcohol craving in those with alcohol dependence may be due to biological differences in brain mechanisms that mediate these euphoriant and anxiolytic effects.

It is often difficult to know whether personality factors are antecedents or consequences of alcohol and drug abuse. However, as noted by Marlatt et al. (1988) and others (e.g., Zucker and Gomberg 1986), a history of antisocial behavior and high levels of depression or low self-esteem have been found in many studies of alcohol and other drug abusers (Cox 1985; Nathan 1988; Tarter, Alterman, and Edwards 1985; Vaillant 1983; Vaillant and Milofsky 1982; Zucker and Gomberg 1986). Nathan (1988) was skeptical about personality as a determining factor in alcohol and other drug abuse, however, partly on the grounds that, although many early behaviors reported to be predictive of later abuse are very prevalent in the general population, most people do not become dependent on alcohol or drugs. In particular, Nathan questioned the predictive value of early antisocial behavior, arguing that a large number of abusers have never displayed antisocial behavior and that many people who show that behavior early in life do not become addicts.

Studies of Expectancies

There is evidence that direct pharmacologic effects alone may not be sufficient for either the development or the maintenance of alcohol and drug abuse (Marlatt and Donovan 1981). Social learning, in which information about the consequences of behavior is transmitted through observation of others as well as through one's own experiences (Bandura 1977), also plays an important role. Such nonpharmacologic contributors include expectations about the direct pharmacologic actions as well as expectations about indirect effects on behavior and social functioning (Zinberg 1984; Adesso 1985; Critchlow 1986; Donovan and Marlatt 1980; M.S. Goldman et al. 1987; Lang and Michalec in press; Oei and Jones 1986).

According to Marlatt and colleagues (Marlatt in press; Marlatt et al. 1988), the most notable and most widely held belief, and therefore expectation, about alcohol is that it is something of a "magic elixir" that can enhance social and physical pleasure, sexual performance and responsiveness, power and aggression, and social competence. The power of expectancy is suggested by research showing that people can experience alcohol-like effects when they only think they have consumed alcohol but have instead consumed a placebo beverage (Abrams and Wilson, 1979; Lang et al. 1975; Wilson 1977; also see reviews by Lang et al. 1983; Marlatt and Rohsenow 1980).

There is evidence (Christiansen et al. 1982; Christiansen and Goldman 1983; Christiansen et al. 1985) that people can acquire expectations about alcohol long before they take their first drink and that these early expectancies are strong predictors of drinking behavior in adolescence as well as of alcohol dependence in adulthood. In comparing adolescent alcohol abusers with demographically similar nonabusing peers, Brown et al. (1987) found that the alcohol abusers expected more positive effects from alcohol. A study by Mann et al. (1987) examined alcohol expectancies among adolescents at high and low risk of future alcoholism and found that high-risk adolescents expected enhanced cognitive and motor functioning and reduced tension, whereas low-risk adolescents expected altered social behavior.

A recent study (Christiansen et al. 1989) measured alcohol expectancies in seventh- and eighth-grade children and compared these expectancies with the children's self-reported drinking onset and drinking behavior a year later. (This comparison was a departure from previous studies in this area, which collected expectancy and drinking data in adolescents at the same time.) The investigators found that five of seven expectancy scores were strongly predictive of initiation, quantity, and frequency of drinking and associated problems in the adolescents a year later. Children at highest risk were most likely to have strong expectancies of social enhancement and to believe that alcohol improves cognitive and motor functioning.

Critchlow (1987) studied the relationship between alcohol-related expectancies and drinking patterns in samples of both college students and the general population. Subjects were given a questionnaire to assess their perceptions of the likelihood of a variety of possible effects from alcohol and the desirability of those effects, as well as to obtain information about drinking habits. In both samples, heavier drinkers were found to have greater expectations of positive consequences of drinking than lighter drinkers and tended to evaluate all drinking consequences more positively.

A factor closely related to expectancies about effects of alcohol is the setting in which it is consumed. Sher (1985), in a study of male social drinkers, found that three factors operating both independently and interactively affected bipolar mood states (e.g., pleasure-displeasure) and various bodily sensations. Salient factors were the pharmacologic effects of alcohol; the expectancies of social and sexual enhancement, assertiveness, and relaxation; and whether the alcohol was consumed in a solitary or group setting. Given the same amount of alcohol, those who drank in a group setting and had strong expectancies of reinforcement from alcohol reported feeling more intoxicated immediately after consumption than all other subjects; these drinkers also differed from the others by scoring higher on the measure of pleasure and on several physiological responses.

Another recent study (Leigh 1987) suggests that people's expectancies about the effects of alcohol on themselves and on others are different. In this study, college respondents and general population samples revealed an expectation that alcohol effects of all kinds, but especially socially unacceptable behaviors, were more likely to be experienced by others than by themselves. Respondents also tended to believe that others were more likely to "feel good" after drinking, but the self-other differences on this expectation were small.

In their review, Marlatt et al. (1988) cited another expectancy about alcohol that may be important in its abuse, namely the expectation that alcohol can help in coping with stress or negative moods. Several studies of alcohol and drug abuse have posited that individuals are more likely to use an anxiolytic drug such as alcohol when they feel unable to cope with problems (Donovan and Chaney 1985; Litman 1986; Marlatt and Gordon 1985; Rollnick and Heather 1982). Marlatt et al. (1988) noted that this type of expectancy, though it appears to have validity, has not been as well researched as the set of positive expectancies embodied in the "magic elixir" notion.

Many studies have found that alcohol expectancies and drinking behavior are correlated, but there have been few studies of how well these expectancies match the drinkers' actual experiences when consuming alcohol. In a study of normal drinkers in both drinking and nondrinking situations, Roehling and Goldman (1987) found that individual subjects reported after a drinking session that their experiences coincided with their expectations of greater relaxation, more fun, and sexiness, although they tended to believe that others in the group had more intensive experiences than themselves. Expectancies of cognitive impairment were not fulfilled, however, possibly because the subjects were given cognitive tasks that were not sufficiently challenging, but more likely because they were not able to recognize cognitive impairment either in themselves or in their cosubjects when under the influence of alcohol (Roehling and Goldman 1987).

It might be supposed that expectancies about the effects of alcohol would mimic the actual pharmacologic effects of alcohol. Research indicates, however, that men's expectations about alcohol do not always mimic its pharmacologic actions. For example, studies measuring penile changes show that alcohol decreases sexual arousal in men (Briddell and Wilson 1976), yet, as noted by Newlin (1987), there is strong evidence in the literature that subjects expecting to receive alcohol display increases in both self-reported and physiological measures of male sexual arousal.

To test the role of expectancies in a controlled manner, Newlin and colleagues (Newlin 1985a,b; 1989) have developed an experimental approach in which subjects are divided into two groups, one receiving an alcohol placebo and the other receiving a nonalcoholic beverage that is not purported to be alcoholic. Thus two conditions are created: expectation of alcohol but none received, and no expectation of alcohol and none received. The design allows an alcohol expectancy effect to be measured against a control condition in which alcohol is neither expected nor received. The expectancy effect measured in these studies was the heart rate. The pharmacologic action of alcohol normally accelerates the heart rate, but it was confirmed in young college men that alcohol expectancy decreased the heart rate (Newlin 1985a). This effect, called the antagonistic placebo response, was not found in women, however. Expectancy of receiving alcohol increased the heart rate in women (Newlin 1989) as alcohol itself would do.

The same experimental design was also used in a study of sons of alcoholics (Newlin 1985b) to test the hypothesis that they would show a greater antagonistic placebo response than sons of nonalcoholics. It was confirmed that an alcohol placebo produced significantly greater reductions of heart rate in the sons of alcoholics. The reductions could not be attributed to differences in baseline heart rate, drinking practices, or personality measures. The sons of alcoholics also reported feeling more "intoxicated" after consuming the placebo drink than the sons of nonalcoholics, suggesting the possible existence of some fundamental differences in the two groups in ability to perceive drug states.

It must be emphasized that these studies were performed with the subjects in a relaxed, stress-free environment. This is important because, although alcohol normally accelerates the heart rate through pharmacologic action, it also can slow the heart rate if the heart is beating faster than normal because of stress. Alcohol in such situations apparently slows the heart rate by alleviating stress, and there is evidence that this effect may reinforce further drinking.

Alcohol and Stress Reduction

Significant reduction in cardiovascular response to stress following alcohol administration is one of the more consistent findings in the literature on alcohol and stress reduction (Cummings and Marlatt 1983; Levenson et al. 1980; Sher and Levenson 1982; Wilson et al. 1980; Zeichner et al. 1983). Sher and Walitzer (1986) investigated the alcohol-stress relationship using both a physiological indicator of stress levels (heart rate) and a psychological measure of anxiety. They found, consistent with earlier research, that alcohol reduced both heart rate and anxiety responses to a stressor. However, in contrast to other studies, this investigation found no evidence that expectancies about alcohol effects played any role in the stress-reduction responses observed in subjects who consumed alcohol.

Levenson et al. (1987) tested a hypothesis that individuals at greater risk for alcoholism tend to get greater reinforcement from drinking because they find it more rewarding. The hypothesis was supported in a comparison of alcohol-induced stress attenuation in high- and low-risk subjects in which the effects of a high dose of alcohol on both physiological (cardiovascular and motor responses) and self-reported psychological effects of stress from aversive stimulation were measured. Although all subjects received the same amount of alcohol on a body weight basis, those judged at risk for alcohol dependence (because they had an alcoholic parent or matched a personality pattern thought to be associated with the development of alcoholism) experienced a smaller response to the stressor after drinking than control subjects who had neither risk factor. The enhanced stress reduction was evident in subjects with either type of alcoholism risk factor, but no additional stress attenuation was seen in subjects who had both risk factors. There were no differences in the responses of male and female subjects at risk.

Finn and Pihl (1987) also measured the effects of alcohol on cardiovascular responses to aversive stimulation. The subjects, all males, were in three groups: those judged at high risk because they had alcoholic fathers and a multigeneration family history of alcoholism, those judged at moderate risk because there was no alcoholism in the generation preceding that of their alcoholic fathers, and those judged at low risk because they had no family history of alcoholism. Before drinking, the high-risk group was found to have greater cardiovascular reactivity to the stressor than the moderate-risk group. After drinking, however, the high-risk group showed a dramatic reduction of cardiovascular response to the stressor, while the moderate- and low-risk groups showed increased reactivity (see fig. 1). The evidence suggested that the greater baseline reactivity to stress and the heightened stress-dampening effect of alcohol in individuals at high risk of alcoholism may make them more disposed to use alcohol in adverse situations.

The similar reactivity of the moderate- and low-risk groups in contrast to the high-risk group

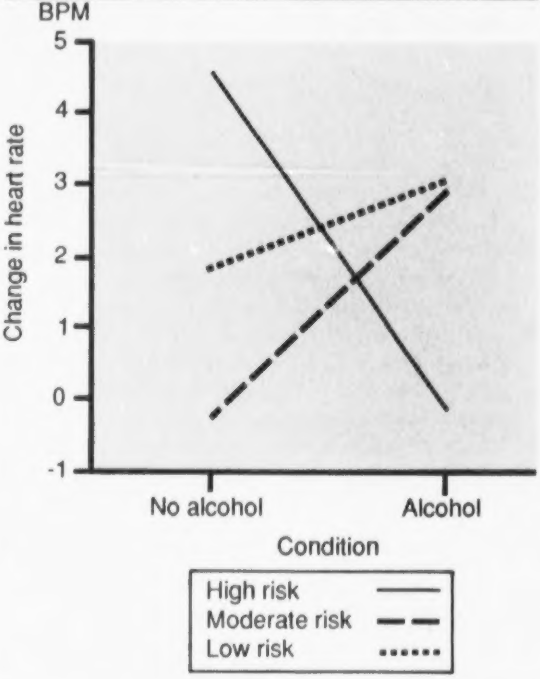

FIGURE 1. Mean change in heart rate in beats per minute (BPM) from resting baseline for high-, moderate-, and low-risk male groups under both no-alcohol and alcohol conditions.
SOURCE: Finn and Pihl 1987. Copyright 1987 by the American Psychological Association.

indicated a need to look more closely at the frequency of alcoholism in an alcoholic family history before judging the risk of alcoholism in any one family member. In a subsequent study by the same investigators (Finn and Pihl 1988), that replicated the findings of the first, it was concluded that investigators should ascertain that familial alcoholism has existed for at least two successive generations before judging an individual to be at risk because of family history. The authors observed that the majority of high-risk studies published have apparently not gone beyond one generation in describing family history of alcoholism.

Longitudinal Studies

The association of parental alcoholism with adverse effects in children is well documented. In reviews of the literature on the impact of parent al alcoholism on offspring (e.g., El-Guebaly and Offord 1977, 1979) numerous authors have cited evidence of negative effects at every age level from prenatal life (the fetal alcohol syndrome and other alcohol-related birth defects) to adulthood. Longitudinal studies of the children of alcoholics have explored childhood factors and their relationship to the development of alcoholism in adulthood.

One such study of children (Werner 1986) focused on factors that allow some offspring of alcoholics to go through childhood and adolescence without developing any serious problems. Asian and Polynesian natives of Hawaii having at least one alcoholic parent and having experienced alcohol-related family problems as children were selected for study; control subjects were from the same cohort of native Hawaiians. Serious problems at home, school, work, or in the community had developed by age 18 in 41 percent of the children of alcoholic parents, and 30 percent had records of repeated or serious delinquency. A striking contrast was found with respect to contacts with social services and mental health agencies; 37 percent of the children of alcoholics had made such contacts during their teens, compared with only 7 percent of the children without alcoholic parents.

The frequency of adjustment problems associated with parental alcoholism was significant in this study. Nevertheless, nearly 60 percent of the offspring of alcoholics had not developed such problems by age 18. Interviews and community records indicated that the members of the resilient group did well in school, at work, and in social life and that they had realistic goals and expectations for the future (Werner 1986). Further evaluation of the resilient and nonresilient children of alcoholics indicated differences in the two groups in temperament, communication skills, and locus of control (i.e., the belief as to whether one's life is controlled by oneself or by external factors). Characteristics differentiating the problem-free offspring of alcoholics from others included relative intelligence, achievement orientation, early social skills, responsible and caring attitude, positive self-concept, and belief in their own effectiveness. One of the factors that most strongly influenced outcome in the children was the presence or absence of alcoholism in the mother; 25 percent of the nonresilient offspring had an alcoholic mother, compared with only 3.5 percent of resilient offspring.

A study in Stockholm (Rydelius 1981) followed for a 20-year period the health and social adjustment in children of alcoholic fathers and control children, all of whom were from families of lower socioeconomic status. A high frequency of health, learning, and social problems was found in the children of alcoholic fathers when they were first studied (at 4 to 12 years of age) and 20 years later. At the time of followup, male children of alcoholics had greater frequency of alcoholism, drug abuse, mental health problems, and antisocial behavior than females.

McCord (1988) reevaluated men who, during their youth, had been interviewed as part of a treatment program to prevent delinquency in a high-risk population. Of the men whose fathers were alcoholic, 47 percent had become alcoholic by middle age, compared with 25 percent of those whose fathers were not alcoholic. Three major factors that differentiated alcoholic from nonalcoholic sons were found: Alcoholic sons tended to come from families in which the father was alcoholic, the mother nevertheless held the father in high esteem, and the son's behavior was beyond the mother's control. The rate of alcoholism in men whose mothers expressed high regard for their alcoholic husbands was nearly double the rate in men whose mothers did not express this high regard. McCord noted, however, that other social and biological factors must be considered in understanding the development of alcoholism.

A longitudinal study by Drake and Vaillant (1988) sought to identify predictors of alcoholism and personality disorders in the children of alcoholics. The study population consisted of males who had been evaluated more than three decades earlier as nondelinquent control subjects in a study of juvenile delinquency (Glueck and Glueck 1950, 1968). At that time, the subjects were adolescents living in high-crime areas of Boston. A review of data gathered when the subjects were adolescents revealed clear differences between the sons of alcoholics and the sons of nonalcoholics. The sons of alcoholics had a greater number of other relatives who were also alcoholic (24 percent versus 13 percent); were more often of non-Mediterranean background (54 percent versus 33 percent); were more likely to have had poor relationships with their mothers (34 percent versus 24 percent) as well as with their alcoholic fathers (58 percent versus 24 percent); and on a variety of measures were more likely to have had poor adjustment, emotional problems, low competence in skills appropriate to their age, and poor physical health. The adolescent adjustment problems were most strongly related to a single variable: a poor relationship with the mother.

At the followup, alcohol dependence, diagnosed by standard clinical criteria, was more than twice as high in the children of alcoholics (28 percent versus 12 percent). Analysis revealed that predictors of eventual alcoholism in the children of alcoholics included the number of alcoholic relatives, ethnicity, and socioeconomic status. School truancy and behavior problems during adolescence were predictive in very few cases (Drake and Vaillant 1988): The investigators reported that their measures of environmental disruption and adolescent adjustment were "remarkably unrelated to subsequent alcoholic drinking" (p. 803). Except for the few subjects who had displayed behavior problems in school, no significant correlations were found between adjustment difficulties in early adolescence and alcoholism in adulthood. Vaillant and his colleagues concluded from their longitudinal studies of these subjects (Vaillant and Milofsky 1982) that behavioral traits and symptoms associated with alcoholism, including antisocial behavior in childhood, are not causes of alcoholism, and that genetic factors probably contribute far more to children's later risk of alcoholism than psychosocial factors associated with their growing up in an alcoholic home.

Zucker and Gomberg (1986) reexamined data reported by Vaillant and Milofsky (1982) and came to different conclusions. Zucker and Gomberg argued that the data of Vaillant and his colleagues, when analyzed by a different statistical technique, revealed a substantial relationship between disturbed adolescence and adult alcohol problems: Children who became alcohol dependent as adults had more behavioral and truancy problems in school, including childhood antisocial behavior, and were more likely to have dropped out of high school. A poor environmental support system and a distant relationship with the father were more common among children who later developed alcohol problems. Zucker and Gomberg also cited several cross-sectional and longitudinal studies that found childhood antisocial behavior to be a significant antecedent of alcoholism (Gomberg 1982; Jessor and Jessor 1977; Zucker and Fillmore 1968).

Zucker and Gomberg (1986) observed, however, that temporal associations among characteristics identified in longitudinal studies do not define causal factors. Nearly all such studies, they noted, have compared individuals at only two points in time, an approach that cannot yield the kind of information needed to trace causal pathways or compare the merits of alternative causal explanations.

Steinglass (1983) discussed methodological problems in family environment studies: In addition to the problem of one-point followup, lack of control groups has been a major deficiency. Jacob and Seilhamer (1987) noted methodological problems in the literature on the impact of parental alcoholism on the psychosocial and psychiatric status of offspring as including overrepresentation of subjects with multiple problems from nonintact families of lower socioeconomic status and overreliance on self-report data. In addition to limiting the ability to generalize findings, design limitations create uncertainty about the developmental patterns involved in adverse outcomes, as well as about the nature of family and nonfamily influences that protect many children of alcoholics from such outcomes (Jacob and Seilhamer 1987).

In summary, many studies have found associations between adult alcohol dependence and circumstances of childhood and adolescence. Yet research to date has been inconclusive about the specific environmental influences involved, and causal roles for any particular family environmental factor in the development of alcoholism remain hypothetical. Nevertheless, some promising areas of inquiry have been identified. These include the question of developmental continuity between social, adjustment, and learning problems in youth and adult alcoholism; issues of parenting; and factors that may protect those at risk from developing alcoholism.

Generational Trends in Familial Alcoholism

Evidence that factors other than familial ones play an important role in the development of alcoholism has come from a recent study (Reich et al. 1988). Investigators found that the frequency of alcohol dependence, especially in alcoholism-prone families, has been increasing, and that the average age of its onset has been decreasing in recent decades. This secular trend has been occurring both in the families of alcoholics and in the general population, suggesting that broad social factors, not just family genetics or family environment, are influencing both kinds of families and increasing the risk of alcoholism.

In the Reich et al. (1988) study, the first-degree relatives and spouses of females and males diagnosed by standard criteria as alcohol dependent were interviewed to determine familial frequency of alcohol dependence and age of onset. For comparison purposes, a similar examination was made of data for the general population in the same area obtained by the Epidemiologic Catchment Area project (Regier et al. 1984).

The trend of increasing frequency of alcohol dependence and declining age of onset was most dramatic when male relatives of alcoholics were compared by age group to determine what percentage of each age cohort had become alcohol dependent by age 20. The analysis showed that in male relatives under 26 years old, the percentage who had become alcohol dependent by age 20 was approximately 52 percent, compared with a 22-percent rate by age 20 in male relatives aged 26 to 44, and a less than 10-percent rate by age 20 in male relatives who were age 45 or older. The percentage of males who had become alcoholic by age 20 was more than 5 times higher in the youngest age cohort than in the oldest. Striking trends were also seen in female relatives of alcoholics. The percentage of female relatives who were alcoholic by age 20 was about 18 percent among those under age 26, compared to less than 5 percent in older cohorts.

These results suggest that the risk for developing alcoholism is greater for younger relatives of alcoholics than for older ones. This study found similar secular trends in the Epidemiologic Catchment Area data, but the trends were not nearly so pronounced as in individuals who have a family history of alcoholism. These changes have occurred too rapidly to be explained by genetic factors, and the fact that these trends are occurring in families with or without a history of alcoholism invites examination of environmental factors that could influence both kinds of families.

At first, these findings may seem inconsistent with indications that overall alcohol consumption rates and frequency of some alcohol problems in the United States have been declining in recent years (see chapter II). Actually, the recent national declines, although gratifying, are relatively small, and the curve of total per capita consumption versus time in the past few years resembles a gently downward sloping plateau, not a precipice. Furthermore, as noted in this and several previous *Special Reports*, a small percentage of drinkers consistently account for a highly disproportionate share of the alcohol consumed in the United States each year. It is not implausible that drinkers in that category could be maintaining or even increasing their consumption while many others are cutting down.

Perspectives on Gene-Environment Interaction

The interaction of genetic factors with psychological and social factors is of fundamental importance in understanding the development of alcohol dependence. As humans are shaped by both genes and environment, future research on alcoholism is likely to focus increasingly on interactive effects and to draw from both biological and behavioral sciences. In pulling together findings from research in several fields to link phenomena such as personality, behavior, and genetic susceptibility to alcoholism, these models may stimulate research that can lead to improved understanding of the causes of alcoholism. Although little is known about mechanisms by which genetic predisposition may come to be expressed in behavior, theoretical perspectives (Tarter, Alterman, and Edwards 1985; Zucker 1986; Zucker and Gomberg 1986; Cloninger 1987) that link personality traits and the risk of alcoholism offer some possible explanations.

In a model proposed by Tarter, Alterman, and Edwards (1985), temperament provides a link between gene and environment in risk for alcoholism among males. Temperament, a constellation of traits involving intensity, speed, and quality of affective and behavioral responsivity, is thought to be hereditary in origin and subject to modification by environmental factors (Allport 1961, cited in Tarter, Alterman, and Edwards

1985). In this theory, temperament trait deviations are said to underlie behavioral factors found associated with male alcoholism. Specifically, factors related to level of activity (high), attention span (diminished), emotional expressivity (labile), ability to calm following stress (slow), and sociability (high) that research has suggested to be characteristic of those vulnerable for alcohol dependence, are thought to be associated with neurological deficits in frontal-midbrain functioning (Tarter, Alterman, and Edwards 1985).

Implications for treatment and prevention, in terms of addressing behavioral manifestations associated with risk are noted. Further, it is suggested that a mismatch between temperament traits that characterize the child and factors in the family environment, particularly the parent-child interaction, may account for findings of associations between childhood home environment and later alcoholism, and may also explain the impact of peer pressure on the drinking decisions of some youths (Tarter, Alterman, and Edwards 1985). Further, it is proposed that the temperament perspective may be useful in the identification of subtypes of alcohol dependence and in the delineation of the gene-environment interaction in the type 2 form (Cloninger 1987). In associating behavioral manifestations with biological origins and social influences, this theory characterizes the development of alcoholism as a "dynamic confluence of numerous organismic and environmental factors" (Tarter, Alterman, and Edwards 1985, p. 350). The authors note limitations to the theory, including the need to include females and to take into account the diversity of the alcoholic population.

Zucker and Gomberg (1986) proposed an integrated theory on the etiology of alcohol dependence that involves biological, psychological, and social processes operating within a developmental framework. Given a genetic causal basis, it is proposed that alcoholism results from a continuous process in which childhood behavior problems and childhood environment play significant roles. The authors cite relevant childhood factors that have been identified through research, including antisocial behavior, achievement deficits, heightened activity level, and interpersonal difficulties of the child; and marital friction, parental deviance, and deficient rearing practices in the family environment.

In this view, the importance of factors that influence behavior is enhanced or diminished on the basis of developmental stage; that is, childhood behaviors and adult alcoholism represent a continuous process in which different social, cultural, and environmental factors are influential at different points of the life cycle (Zucker and Gomberg 1986). Thus, four specific classes of factors—physiological factors and other individual influences, sociocultural and environmental factors, familial factors, and peer influences—interact in the development of drinking behaviors (Zucker 1986). In order to understand the etiology of alcoholism fully, however, Zucker (1986) observed that discontinuities in the developmental process (e.g., instability of drinking behaviors over time) must also be considered.

Cloninger's (1987) integrated theory on the etiology of alcoholism is based on an earlier adoption study (Cloninger et al. 1981). Two clinical alcoholic subtypes that differ in age of onset, drinking behavior, and personality traits are identified (see table 1). Originally defined in terms of patterns of inheritance, type 1 (milieu-limited) involves genetic factors and strong environmental influences, whereas type 2 (male-limited) is highly heritable with limited environmental involvement, and is associated with both parental alcoholism and parental antisocial behavior (Cloninger et al. 1981). Additional differentiation has recently been suggested in relation to vulnerability for key symptoms related to each type: psychological dependence on alcohol (i.e., loss of control) in type 1, and spontaneous alcohol-seeking (i.e., inability to achieve complete abstinence) in type 2. Other differentiating drinking variables include guilt about drinking in type 1, and drinking-involved aggressivity and law involvement in type 2 (Cloninger 1987).

Furthermore, Cloninger (1987) proposed three traits—novelty seeking, harm avoidance, and reward dependence—that together describe subtype personalities. According to this perspective, type 1 involves behaviors consistent with a "passive dependent" personality, including inflexibility and contemplative behavior (low novelty seeking), careful and inhibited behavior (high harm avoidance), and concern about the feelings and thoughts of others (high reward dependence); type 2, on the other hand, involves behaviors consistent with antisocial personality, including impulsivity and excitability (high novelty seeking), brash and uninhibited behavior (low harm avoidance), and distant social relations (low reward dependence) (Cloninger 1987). Type-specific physiological differences related to P3 amplitudes (Begleiter, Porjesz, Rawlings, andEckardt 1987) and platelet MAO levels (von Knorring et al. 1985, 1987) were discussed earlier in this chapter.

TABLE 1. Distinguishing characteristics of two types of alcoholism

Characteristic features	Type of alcoholism	
	Type 1	Type 2
Alcohol-related problems		
Usual age of onset (years)	After 25	Before 25
Spontaneous alcohol-seeking (inability to abstain)	Infrequent	Frequent
Fighting and arrests when drinking	Infrequent	Frequent
Psychological dependence (loss of control)	Frequent	Infrequent
Guilt and fear about alcohol dependence	Frequent	Infrequent
Personality traits		
Novelty seeking	Low	High
Harm avoidance	High	Low
Reward dependence	High	Low

SOURCE: Cloninger 1987. Copyright 1987 by the AAAS.

Cloninger (1987) noted, however, that the typology does not represent an absolute differentiation, but rather opposite ends of a spectrum of characteristics that may be displayed in differing degrees by individual alcoholics. Given the heterogeneity of the alcohol-dependent population, the utility of identifying specific subtypes is clear.

The systematic study of gene-environment interactions in the etiology of alcoholism has barely begun. It is encouraging, however, that researchers in the field are beginning to draw on knowledge from both the biological and the psychosocial literature on alcohol-related behaviors to formulate gene-environment hypotheses that can be tested.

In science the boundary areas between disciplines often prove to be rich sources of new knowledge and dramatic advances in understanding. In the future, there doubtless will be great opportunities for cooperation between geneticists and environmentalists and exciting prospects for advances in our understanding of the causes of alcoholism.

Summary

There is a wealth of evidence that one of the greatest risk factors for becoming an alcoholic is to be the son, daughter, or sibling of one. The familial nature of alcoholism has stimulated a great deal of research to identify the causes and mechanisms of the transmission of alcoholism in families. In general, these investigations focus on genetics, psychological and social factors, or the interaction of the two. Research indicates that both genetics and environment are involved in the development of alcoholism and alcohol abuse.

A causal role for genetics is supported by human twin and adoption studies, studies of selectively bred animal lines that differ genetically in a number of alcohol-related traits such as alcohol preference, studies of genetically controlled physiological and biochemical characteristics that appear to precede the development of alcoholism in individuals judged to be at risk because of family history, and studies of genetic variations in alcohol metabolism that seem to provide some degree of protection against alcoholism in certain populations.

Psychological and social factors influence drinking behaviors, and research is continuing on the environmental factors involved in the development of alcohol dependence. These factors include the pharmacologic effects of alcohol; the psychological state of the user, especially expectations about alcohol's effects; and the characteristics of the setting in which alcohol is used. Positive expectations about alcohol's effects appear to be significantly involved in initiation to drinking, the continuation and frequency of drinking, and the reasons for drinking. Several studies show correlations between alcoholism and environmental conditions in early life and adolescence that appear to affect personality development, particularly in association with parental alcoholism.

Adoption studies have identified two types of alcoholism, type 1 (milieu-limited) and type 2 (male-limited). Milieu-limited alcoholism is influenced by genetic predisposition and environmental factors. Male-limited alcoholism is highly heritable and influenced very little by environment. Three personality traits—novelty seeking, harm avoidance, and reward dependence—are thought to distinguish the two types of alcoholism.

Evidence of the importance of factors other than familial ones comes from a recent study that discovered a steady increase in frequency of alcoholism and a decrease of the age of onset in comparing different age cohorts. Younger cohorts had a higher prevalence of alcoholism than older ones, and they became alcohol dependent earlier. These secular trends, which are seen in the general population as well as in the relatives of alcoholics, suggest that broad social factors are influencing the risk for alcoholism.

The interaction of genetics and environment is a fundamentally important issue in the development of alcoholism, and future research on alcoholism will focus increasingly on this interaction.

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Chapter IV

Neuroscience

Introduction

Keys to understanding why people abuse alcohol and why some become alcohol dependent lie in neuroscience research. Investigations in this multidisciplinary field are progressing toward explaining how the effects of the environment interact with individual genetic makeup to influence the networks of brain molecules and cells that in turn determine our behavior. In neuroscience research, methods are becoming available to explore the mechanisms underlying such complex biological and behavioral responses as alcohol intoxication, reinforcement, tolerance, and dependence. The reinforcing properties of alcohol and its pharmacologic effects have been considered to contribute to the generation of pathological drinking behavior. Tolerance (changes in the brain's sensitivity to alcohol after repeated use) and physical dependence (the occurrence of physiological withdrawal symptoms when alcohol intake is abruptly terminated) are observed in both animals and humans after chronic ingestion of high doses of alcohol. Recent studies have provided interesting new information about the neural events that may mediate alcohol intoxication, and important clues for understanding alcoholism. Specifically, these studies are producing a better understanding of the effects of alcohol abuse in terms of the "receptive areas" for alcohol in nerve cell membranes, the multiple chemical messenger systems involved in mediating alcohol's actions, the regions of brain circuitry that are most vulnerable to alcohol, and the behaviors associated with these modifications in brain chemistry and physiology.

The effects from short-term or acute exposure to alcohol on the brain are discussed in this chapter in the "Acute Effects" section. At low doses, acute effects may include alterations in mood, cognition, anxiety level, and motor performance; at higher doses, alcohol may induce sedation and anesthesia. The "Chronic Effects" section reviews the consequences of long-term or chronic exposure to alcohol and discusses recent evidence about the processes of tolerance and dependence. Advances in our knowledge of alcohol's reinforcing properties are discussed in the "Behavioral Measures" section. In the last section, "Alcohol Effects on the Human Brain," new studies showing the pathological effects of alcohol on the human brain are reviewed.

Acute Effects of Alcohol

To affect brain chemistry and function, alcohol molecules cross from the bloodstream into the brain and interact with brain cell membranes. Like other cell membranes of the body, brain cell membranes act as effective barriers between the inside and the outside of cells and allow only selected ions, water, and molecules to enter. Cell membranes, however, are permeable to alcohol. Further, cell membranes of the central nervous system (CNS) have the additional property of conducting electrical signals based on the flow of negatively and positively charged ions across cell membranes. Brain cell membranes are composed of lipids, which are arranged in a bilayer with polar heads facing the outer surfaces and nonpolar fatty acid chains facing inward, and proteins, which are intercalated in the lipid matrix and serve as the functional moieties of the membrane (see fig. 1).

Many drugs, such as the opiates, affect the brain by interacting with specific protein constituents of brain cell membranes. These proteins include what are referred to as "receptors," which are complex structures with sites to recognize and bind transmitter substances or interact with particular enzymes, and "channels," which are structures that form functional pores in the membrane through which specific ions can flow. In contrast to the opiate drugs, alcohol's actions on brain cell membranes are less defined. One long-standing hypothesis, referred to as the "membrane hypothesis," proposes that alcohol acts as a nonspecific membrane perturbant, altering the physical properties of the lipid components of brain cell membranes and changing membrane "fluidity" (Meyer and Gottlieb 1926; Chin and Goldstein 1977a).

Research has demonstrated that the membrane hypothesis may help explain how very high doses of alcohol act to sedate or anesthetize individuals (Lyon et al. 1981). For a long time, however, it was uncertain how alcohol affected the brain at the lower doses, producing effects such as euphoria or anxiety reduction. Now, there is exciting new research demonstrating that these effects of alcohol may indeed be mediated by specific receptive areas within the brain cell membrane. This research shows, for example, that specific regions of neuronal membranes show selective sensitivity to even low doses of alcohol, suggesting that various membrane-bound proteins, which are nonetheless dependent on the immediately surrounding lipids for optimal activity, are particularly sensitive to alcohol (Tabakoff and Hoffman 1987).

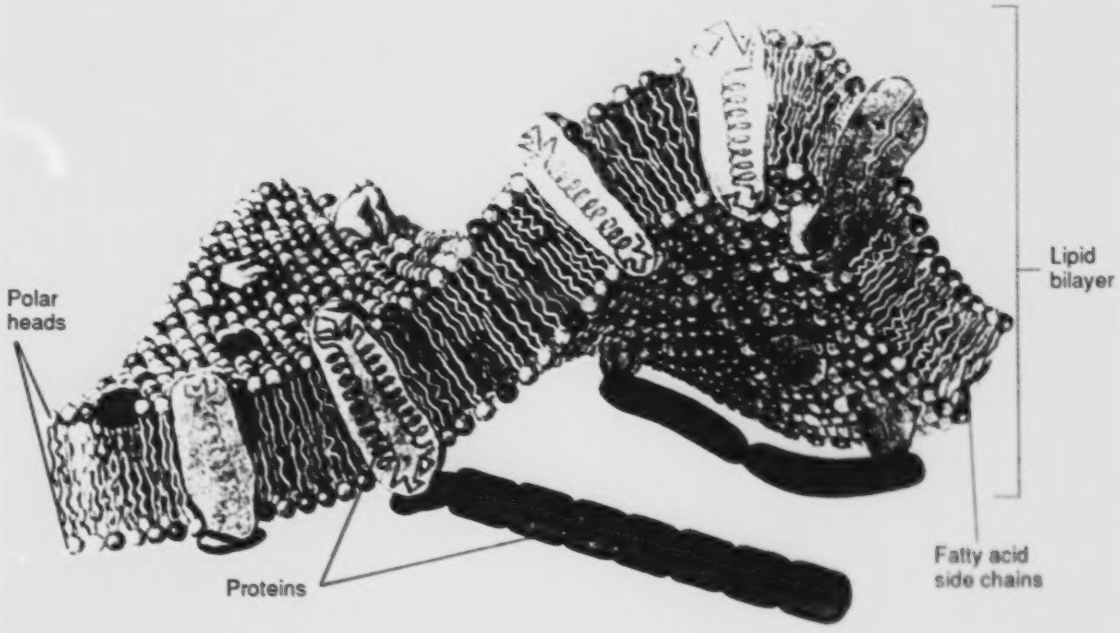


FIGURE 1. Model of nerve cell membrane.
SOURCE: Gallaher 1989. Illustration copyright 1989 by Sally Bensusen.

Brain Processes and Research Methods

To understand abnormal brain functioning, it is important first to review current notions of normal brain activity. Parts of brain cell membrane that are critical for normal brain function are those at synapses. Synapses are the contact zones between two brain cells (neurons) where information from one neuron is transmitted to a second, as illustrated in figure 2. In general, a bioelectrical signal is first conveyed down the length of a neuron until it reaches the cell terminal area, a specialized region where neurotransmitter molecules are stored. There, with the help of certain ions the activation of which is sensitive to the bioelectric signal (for example, the voltage-sensitive calcium ions), neurotransmitter packets are mobilized for transport into the synapse. If the apposed second neuron in the chain recognizes appropriate neurotransmitter molecules by means of receptors, selective ion channels or enzymes can be activated, which, in turn, can lead to a chain of molecular and cellular events, including the propagation of information toward yet a third neuron. There is evidence that alcohol acts in a dose-dependent manner (that is, within a physiologically relevant range, the more alcohol added, the more pronounced the effect is) to affect neuronal excitability at various stages of this process (Siggins et al. 1987).

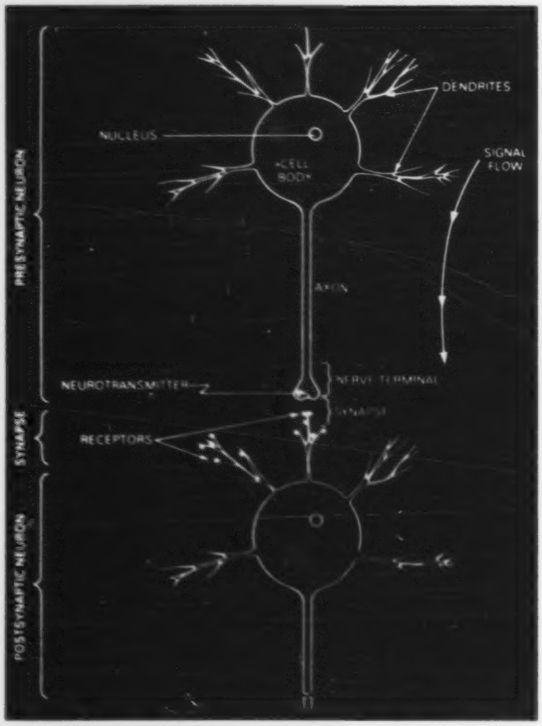


FIGURE 2. Typical nerve cell.
Provided by Dr. Boris Tabakoff.

A variety of techniques are being used to study how alcohol affects brain biochemistry and behavior. The in vivo techniques use humans or animal models to measure parameters such as changes in brain electrical activity, levels of neurotransmitters in certain brain regions, and responses to alcohol under certain experimental conditions. One promising approach has been to record neuronal activity arising in response to alcohol in freely moving, unanesthetized animals with implanted electrodes (Chapin and Woodward 1989). This approach eliminates confounding factors caused by interactions between alcohol and anesthetics and makes it possible to translate alcohol's actions at the cellular level into specific behavioral effects. Other in vivo techniques rely on new imaging technologies such as computerized tomography (CT) and positron-emission tomography (PET) to examine structural and metabolic changes in brain activity after acute or chronic alcohol consumption. These studies are being performed both in animals (Marietta et al. 1986; Eckardt, Campbell, et al. 1988) and in humans (e.g., Pfefferbaum et al. 1988). Also, researchers have been using rodent lines that have been selectively bred with specific sensitivity to the effects of alcohol, to explore genetically mediated biochemical correlates of behavior (Crabbe 1989).

In contrast to the in vivo procedures, in vitro (literally, in glass) methods involve the use of cellular components and tissues isolated from humans or animals.

One in vitro technique uses slices of particular areas of the brain (such as the hippocampus, which is a structure deep in the temporal lobe) to study biochemical and physiological effects of alcohol. In another in vitro technique, brain cells are isolated and maintained in specialized cell-culture fluid media. In cell culture, the effects of alcohol on the activity of individual ion currents in selected patches of membrane can be recorded electrophysiologically (e.g., patch-clamp techniques). Many of the characteristics of nerve cells in the intact brain are retained in these cultures, including excitability, ability to link physiologically with other nerve cells, and ability to synthesize neurotransmitters.

In vitro approaches also include the study of subcellular components of brain cells such as synaptosomes, which contain only those regions of the nerve cell apposed to synapses. This method allows researchers to understand the effects of alcohol on the nervous system in isolation from possible confounding systemic factors (Scott et al. 1986; Acosta et al. 1986).

Because both in vivo and in vitro studies are each subject to limitations, it is clear that both approaches are needed to obtain a clearer picture of alcohol's effects on the CNS.

The GABA Receptor/Chloride Channel Complex

Recently, there has been considerable interest in alcohol's interactions with gamma-aminobutyric acid (GABA), the major inhibitory neurotransmitter of the mammalian brain. GABA-ergic activity has been studied in many areas of the brain that are sensitive to the effects of alcohol, including the cortex, striatum, hippocampus, and cerebellum. It has been proposed that some of the biochemical and behavioral effects of alcohol may be due to the enhancement of inhibitory neurotransmission, probably mediated by the GABA receptor (Celentano et al. 1988; Glowa et al. 1989). Some studies (Majewska 1988) suggest that alcohol affects GABA's ability to bind to the receptor complex or to cause changes in GABA metabolism, two responses that would provide strong evidence for the role of alcohol in enhancing GABA neurotransmission (Greenberg et al. 1984; Hoffman et al. 1987). However, several studies that have examined GABA activity using electrophysiological techniques have not been able to document any effect of alcohol (Mancillas et al. 1986; Siggins et al. 1987), while several studies have reported effects (e.g., Nestoros 1980). In addition, it recently has been reported that neither low nor high doses of alcohol changed the rate or the net amount of GABA used in various regions of the brain (e.g., substantia nigra) relative to control areas, suggesting that alcohol may not produce changes in the availability of GABA in presynaptic nerve terminals (Frye and Fincher 1988).

How, then, might alcohol effect GABA neurotransmission? The GABA receptor is a complex protein that has recognition sites for GABA, barbiturates, and benzodiazepines (tranquilizers, e.g. Valium) that produce many effects similar to those of alcohol; indeed, the GABA receptor is sometimes referred to as the GABA-benzodiazepine receptor (Squires 1988). It has been well established that one type of GABA receptor, the GABAa receptor, is coupled to the opening of chloride ion channels (Olsen 1982). There is now considerable evidence from studies that have employed electrophysiological recording techniques, as well as from biochemical studies that have used subcellular brain fractions, that alcohol may also affect the GABAa receptor chloride channel, causing a greater influx of this negatively charged ion into the cell (Allan and Harris 1986; Mereu and Gessa 1985; Schwartz et al. 1986; Mehta and Ticku 1988). Not all electrophysiological studies, however, have been able to document alcohol's effects on GABA-activated chloride flow (Barker et al. 1987). One recent study showed that, in isolated cells, there was a strong correlation between the effects of infusing a series of alcohols that were graded for their ability to produce intoxicating effects (including ethanol, which is present in alcohol beverages) and their ability to enhance GABA-stimulated chloride flux (Suzdak et al. 1988). This study provided additional evidence for some of the effects of alcohol being mediated by the GABA receptor system.

Studies suggest that at low concentrations, alcohol may exert its effects by potentiating the effects of GABA-mediated chloride flux. Some investigators (Suzdak et al. 1988; Mehta and Ticku 1988) but not all (Allan and Harris 1986) have found that at higher concentrations alcohol may activate chloride channels directly. Schwartz et al. (1986) suggested that these alcohol effects are mediated by means of an alteration in the lipid-protein microenvironment of the GABA receptor/chloride channel complex. Another recent study has suggested that alcohol may affect glycine neurotransmission (another major inhibitory neurotransmitter in the brain) in a similar manner, i.e., through alterations in glycine-activated chloride channel activity (Celentano et al. 1988).

One way to demonstrate that a specific process, such as chloride flux, is responsible for mediating an effect on the brain, such as alcohol intoxication, has been to find a chemical substance that will specifically block that effect. Over the past few years, a compound called Ro15-4513, a partial inverse agonist at the GABA-benzodiazepine receptor, has been shown to antagonize specific biochemical and behavioral effects of alcohol (Suzdak, Glowa, et al. 1986; Bonetti et al. 1985; Polc 1985; Hoffman et al. 1987). Unlike antagonists, inverse agonists do not simply reverse the effects of a pharmacologic agent, but have the exact opposite effects of that agent. For instance, Ro15-4513 and similar agents do not simply block the effects of benzodiazepine anxiolytics like Valium, but produce anxiety and stress when given alone. Harris et al. (1988) reported that both Ro15-4513 and another inverse agonist, FG 7142, blocked GABA-activated chloride flux in an isolated mouse brain membrane preparation. In one recent electrophysiology experiment, both Ro15-4513 and FG 7142 were shown to block the depressive effects of alcohol on the cerebellum, an area of the brain associated with balance and movement (Palmer et al. 1988). Thus from biochemical and electrophysiological studies it appears that Ro15-4513 can be used in some cases to provide clues about the site of some of alcohol's actions, even though it does not appear able to block all of alcohol's acute effects.

Alcohol also has been reported to potentiate certain of the behavioral effects of GABA. In order to assess whether an antagonist is blocking behaviorally relevant actions of alcohol, investigators have used animal models and measured functions that are normally altered with alcohol consumption, such as changes in anxiety, temperature regulation, motor coordination, and sedation. Using a rat model to study the tension-relieving actions of alcohol, Koob et al. (1988) recently reported that at low doses a substance called isopropylbicyclophosphate, which binds to the GABA receptor, reversed some of the anxiolytic effects of alcohol ingestion. This same group reported that Ro15-4513 blocked some of alcohol's anxiolytic and intoxicating properties (Koob et al. 1989). Lister (1989) demonstrated some specificity in the behavioral effects of alcohol on the GABA-benzodiazepine receptor by showing that Ro15-4513 blocked anxiolytic and exploratory behaviors but did not change the increased locomotor stimulation that is observed after alcohol administration. Unfortunately, Ro15-4513 increases anxiety and seizure activity in the brain and is unlikely to be useful as a clinical agent (Ticku and Kulkarni 1988; Lister and Nutt 1988).

There has been some suggestion that the GABA neurotransmitter-receptor system may be differentially responsive to the effects of alcohol in animals that have been genetically bred for their behavioral responses to alcohol. One line of genetically bred mice that may be relevant to understanding the anxiolytic effects of alcohol on the GABA-benzodiazepine receptor complex has been bred based on some animals' resistance to a particular benzodiazepine, diazepam; these mice are referred to as diazepam resistant (DR) and diazepam sensitive (DS) (Gallaher et al. 1987). Indeed, the DS mice were found to be more sensitive to the behavioral effects of alcohol on motor coordination and also took longer to recover after intoxication than the DR mice (Gallaher and Gionet 1988). Genetically bred rat lines also have been established based on preference for alcohol. These animals (P rats) voluntarily drink ethanol solutions, develop tolerance and physical dependence with chronic drinking, and work to obtain alcohol independently of alcohol's caloric value, taste, or smell. Their counterparts, known as nonpreferring (NP) rats, are characterized more by avoidance of alcohol (for further discussion, see chapter III). Ro15-4513, and hence the GABA neurotransmitter system, appeared to affect alcohol intake but not food or water intake in both the P and NP rats, suggesting an association of GABA with alcohol drinking. However, because alcohol intake was reduced in both P and NP strains, it was proposed that a neurotransmitter system other than GABA (perhaps serotonin) is involved in establishing or reinforcing preference for alcohol over water (McBride et al. 1988).

Other studies have been conducted using the genetically bred, long-sleep (LS) and short-sleep (SS) mouse lines. These mouse lines were developed after it was found that the LS mice were more sensitive to even small doses of alcohol than the SS mice (Crabbe 1989). LS mice also have been found to be more sensitive than SS mice to the administration of various GABA-like substances (Marley, Freund, and Wehner 1988). This differential response of LS and SS mice has been attributed to molecular and conformational differences between the strains in the GABA-benzodiazepine receptors (Marley, Stinchcomb, and Wehner 1988).

Many recent biochemical, behavioral, and genetic studies suggest interactions between alcohol and the GABA neurotransmitter and receptor system. Discrepancies between studies on the effects of alcohol on GABA-mediated chloride flux point out the need to explore further the molecular mechanisms underlying the activation, modulation, and regulation of ion channels; as with other chemical substances, the effects of alcohol may be dependent on the state of the brain cells at the time of testing (Kaczmarek and Levitan 1987). Over the past few years, research in this area appears to be progressing from descriptive studies of alcohol's effects on particular neurotransmitters, such as GABA, to mechanistic studies on how alcohol might be interfering with normal brain functions.

Glutamate, the NMDA Receptor, and Calcium Channels

A number of exciting findings have been reported that suggest that another neurotransmitter-receptor system, the glutamate system and especially its N-methyl-D-aspartate (NMDA) receptor, may be mediating many of the acute effects of alcohol. The activity of glutamate (an amino acid which appears to be the main excitatory neurotransmitter of the mammalian brain; Watkins and Olverman 1987) has been shown to be affected by alcohol (Michaelis et al. 1987). Findings that alcohol inhibits the activity of glutamate (inhibiting excitation) complement reports that show alcohol to potentiate the activity of GABA (increasing inhibition). Glutamate produces its excitatory action through at least three types of receptors, designated kainate, quisqualate, and NMDA, based on their responses to these compounds that mimic the effects of glutamate (Watkins and Olverman 1987). Recent studies showed that alcohol affects glutamate neurotransmission specifically at the NMDA receptor (Lovinger et al. 1989; Hoffman et al. 1989).

The NMDA receptor has been investigated in some detail (Foster and Fagg 1984; Mayer and Westbrook 1987). Relevant to the effects of alcohol intoxication, the NMDA receptor is thought to be involved in memory functions through a process called "long-term potentiation" (Harris, Ganong, and Cotman 1984). Long-term potentiation refers to changes in neuronal biochemistry and physiology that perpetuate brain signals long after signals evoked through neurotransmission have decayed. It has been demonstrated that even moderate amounts of alcohol impair learning and memory processes that could involve the NMDA system (Lister et al. 1987). In addition, aberrant activation of the NMDA receptor appears to play a role in hypoxic damage and epileptiform seizure activity (Simon et al. 1984; Dingledine et al. 1986; Kauer et al. 1988). Understanding alcohol's actions at the NMDA receptor, then, might help explain the seizures that often accompany alcohol withdrawal. Other studies have shown the importance of the NMDA receptor during brain cell growth and development (Pearce et al. 1987). Changes in the normal functioning of the glutamate-NMDA system then could possibly explain aspects of the impairments seen in fetal alcohol syndrome.

A number of reports have shed some light on how the NMDA receptor functions. Ascher and Nowak (1986) found that NMDA receptor-gated channels, when open, are permeable to calcium ions, as shown in figure 3. It was also found that NMDA actions are selectively blocked by the street drug phencyclidine (PCP or "angel dust") (Anis et al. 1983). Furthermore, it has been shown that glycine, an inhibitory neurotransmitter, enhances the actions of NMDA (Johnson and Ascher 1987).

Several groups of investigators have reported on the effects of alcohol on NMDA-receptor activity. In an electrophysiological study of hippocampal cells in culture, Lovinger et al. (1989) recently demonstrated the effect of even very small amounts of alcohol on NMDA ion currents. First, they were able to show that alcohol reduced NMDA ion currents in a dose-dependent fashion (see fig. 4a). Second, they showed that the potency for reducing the NMDA currents by a series of graded alcohols, including ethanol, was related to the potency of these alcohols' intoxicating effects (see fig. 4b). These two complementary results strongly suggest that alcohol's inhibition of responses at the NMDA receptor may contribute to the cognitive impairments associated with intoxication.

In a study using primary cultures of cerebellar cells, Hoffman et al. (1989) reported that NMDA stimulated calcium uptake in a dose-dependent manner and that alcohol strongly blocked the NMDA-stimulated calcium uptake. Further, it has also been shown that alcohol administration will block long-term potentiation induced by calcium in the hippocampal slice (Sinclair and Lo 1986). This study contributes additional evidence that long-term potentiation might be mediated by calcium flux at the NMDA receptor.

In several neurotransmitter systems, alcohol has been shown to alter other cellular processes by affecting the activity of enzyme systems involved in the generation of "second messengers" (Rabin and Molinoff 1981; Stenstrom and Richelson 1982). For example, there is recent evidence that alcohol may interfere with one particular second messenger, viz., cyclic guanine monophosphate (cGMP) at the NMDA receptor. cGMP is involved in the regulation of cellular metabolism and its production is stimulated by NMDA (and glutamate) (Novelli et al. 1987). Alcohol appears to block NMDA-mediated

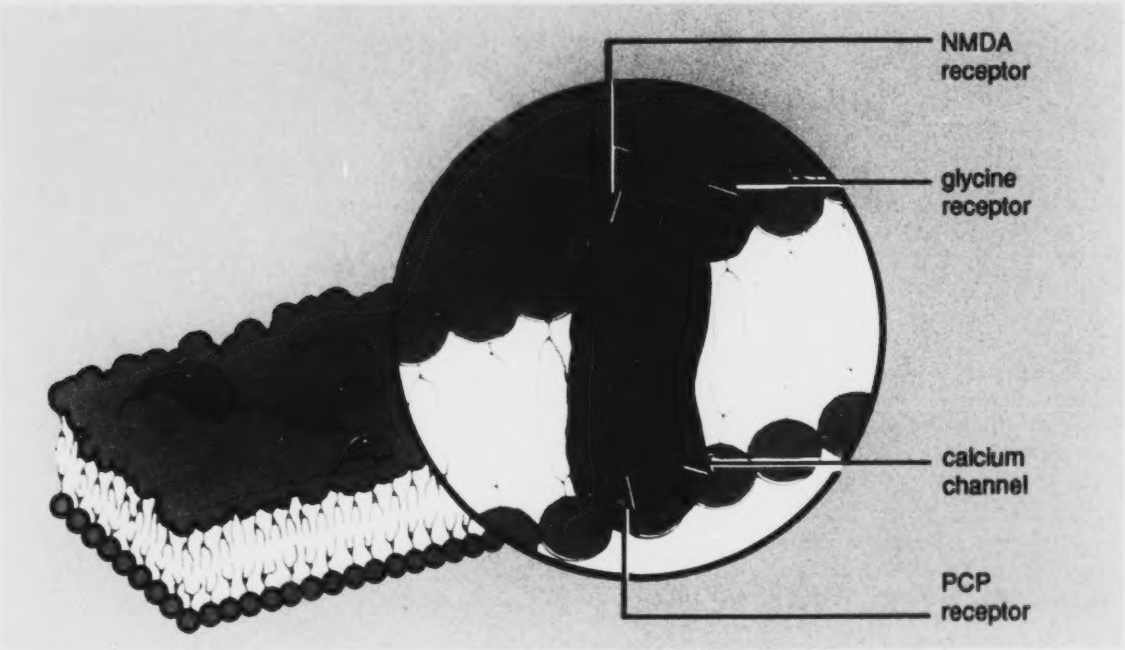


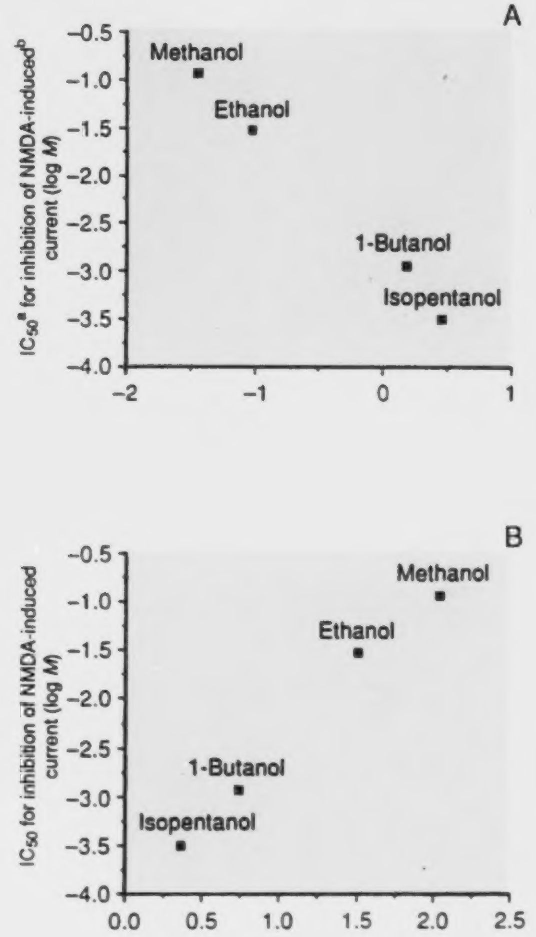
FIGURE 3. Model of N-methyl-D-aspartate receptor.
Provided by Dr. Boris Tabakoff.

cGMP production (Hoffman et al. 1989). Prior studies had already indicated that intoxicating doses of alcohol lowered brain cGMP levels (Hunt et al. 1977) and that this effect was most pronounced in the cerebellum (Volicer and Klosowicz 1979; Ferko et al. 1982). This additional evidence implicates the NMDA system in cGMP changes after alcohol ingestion.

Another plausible mechanism is that alcohol appears to block the ability of glycine to enhance activity of NMDA-mediated cGMP (Hoffman et al. 1989). This likelihood is interesting because both biochemical and electrophysiological experiments have indicated that glycine may play a role as a co-agonist at the NMDA receptor (Johnson and Ascher 1987; Kleckner and Dingledine 1988). Together, these results suggest that the concomitant activation of glycine and NMDA receptors, which may reflect the normal pattern of activation, may be an event that is particularly sensitive to the presence of alcohol. Although there have been reports that increases in intracellular calcium levels (which theoretically could be mediated by NMDA receptor activities) may be important for modulating the activity of GABA receptor chloride channels (Inoue et al. 1986), it is uncertain at present whether there is an important mechanistic relationship between alcohol's effects on the GABA and glutamate systems (Hoffman et al. 1989).

An Important Second Messenger System: Cyclic Adenosine Monophosphate

In searching for molecular mechanisms that might explain alcohol's acute effects on the brain, there has been great interest recently in understanding processes that might be common to several neurotransmitter systems. In this regard, the adenylate cyclase (AC) system has been receiving much attention (Bode and Molinoff 1988; Mochly-Rosen et al. 1988; Saito et al. 1987). AC regulates intracellular levels of cyclic adenosine monophosphate (cAMP). In addition to its other actions on intracellular processes, cAMP also affects the molecular synthesis of RNA and of proteins in other cell systems, and thus its proper functioning has important long-term consequences for cellular well-being. Studies with neuroblastoma cell cultures have shown that alcohol changes the production of cAMP and prostaglandins (Stenstrom and



FIGURES 4A and 4B. Relation between the potency of different alcohols for inhibiting the NMDA-activated ion current, the hydrophobicity (extent to which alcohols mix with water) of the alcohols, and the potency of the alcohols for producing intoxication. Ethanol is the alcohol present in alcoholic beverages.

A. Relation between inhibition of NMDA-activated currents and the membrane buffer partition coefficient (the affinity to alcohol versus water).

B. Relation between ED3[c] for intoxication and the IC_{50} values for inhibition of the NMDA-induced currents by the alcohols.

[a] IC_{50}: amount of ethanol required to inhibit the NMDA response 50 percent.

[b] NMDA: N-methyl-D-aspartate.

[c] ED3: dose of ethanol that will produce a rating of 3 on the Majchrowitz intoxication scale.

SOURCE: Lovinger et al. 1989. Copyright 1989 by the AAAS.

Richelson 1982). Hoffman and Tabakoff (1986) demonstrated that the effects of alcohol on the AC system were different from those of other drugs such as the opiates. As noted in chapter III, there is evidence that variations in AC may be a marker for the genetic risk for alcoholism. Stimulation of AC activity by acute alcohol administration has been observed in several peripheral organs (Gorman and Bitensky 1970; Uhlemann et al. 1979), in the brain (Rabin and Molinoff 1981, 1983; Luthin and Tabakoff 1984; Saito et al. 1985), and in cultured nerve cells (Gordon et al. 1986).

Three linked components—the receptor, a regulatory protein that is guanine-nucleotide dependent and often referred to as a G protein, and the catalytic unit of AC—contribute to the expression of AC activity (Stadel et al. 1982). These components are presumed to reside on the inner leaflet of the brain cell membrane in close proximity to each other, comprising a coupled system (see fig. 5). It has been suggested that in different areas of the brain, alcohol may interfere with different components of the AC system (Tabakoff and Hoffman 1987).

Some studies have considered that the receptors, acting as the recognition sites for neurotransmitters and other substances that modulate AC activity, may be the critical site for alcohol's effects on the AC system. In the striatum, an area of the brain that has been implicated in motor and cognitive brain circuitry, the neurotransmitter dopamine (DA) was reported to stimulate AC activity at its receptors by interacting with the G protein and the AC catalytic enzyme. In these studies, alcohol was shown to potentiate the effects of DA-stimulated AC activity (Rabin and Molinoff 1981; Luthin and Tabakoff 1984). In the cerebral cortex, the neurotransmitter norepinephrine, through the activation of beta-adrenergic receptors, appears to have multiple sites of action on the AC complex (Saito et al. 1985; Rabin and Molinoff 1981; Tabakoff et al. 1984; Bode and Molinoff 1988). Alcohol has been shown to alter the ability of norepinephrine-like substances to bind to cortical beta-noradrenergic receptors and to activate AC activity (Valverius et al. 1987).

The receptor for adenosine is another site suggested to mediate both acute and chronic effects of alcohol, through the AC second messenger system. Using selectively bred LS and SS mice, Proctor and Dunwiddie (1984) first demonstrated

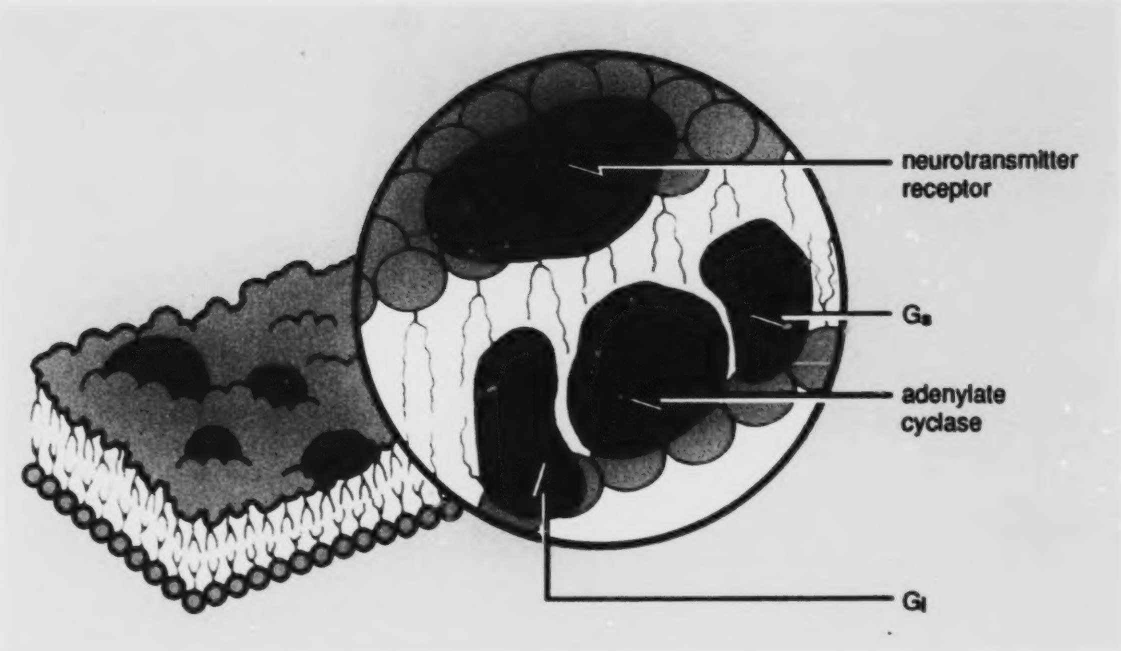


FIGURE 5. Model of adenylate cyclase system.
Provided by Dr. Boris Tabakoff.

that LS mice, which are more sensitive to the sedating and hypothermic effects of alcohol than SS mice, were similarly more sensitive to substances that activate the adenosine receptor. Alcohol was also found to increase adenosine receptor-stimulated cAMP levels in cloned neural cell lines (Stenstrom et al. 1985; Gordon et al. 1986). Recent studies exploring the long-term effects of adenosine-stimulated AC activity at the adenosine receptor are proving this to be a fertile area of investigation. Studies have shown that after long-term exposure to alcohol, cultured neural cells adapt to the presence of alcohol and show a reduction in adenosine receptor-stimulated cAMP levels. After chronic exposure to ethanol, the cells require alcohol to achieve normal levels of adenosine receptor-stimulated cAMP. This process, then, may indicate a form of cellular "dependence" on alcohol (Diamond et al. 1987).

Activation of the appropriate receptors causes changes in the regulatory G protein, and these changes, depending on the specific regulatory protein involved, may either stimulate or inhibit AC. Alcohol's effects on the G proteins are of particular interest at this time, especially on the protein known as Gs, which stimulates AC activity in the presence of guanine nucleotide or analogous compounds. Another regulatory protein, Gi, has an inhibitory influence on AC when the receptor is activated, but this protein does not appear to play a role in the alcohol-induced alterations in AC activity (Hoffman and Tabakoff 1986). In a recent study designed to localize alcohol's most important actions at the AC complex, a number of agents were used to block particular aspects of AC activity (Bode and Molinoff 1988). The results of this study indicated that alcohol's stimulation of AC was due to the enhanced activation of Gs and/or to the coupling between Gs and the catalytic component of the enzyme.

Alcohol also has been shown to potentiate the actions of a neuropeptide known as somatostatin (Mancillas et al. 1986). The actions of somatostatin also are coupled to activation of a G protein (Aktories et al. 1983; Reisine et al. 1985). Somatostatin is found in the hypothalamus; effector sites are in many areas of the brain including the striatum, hippocampus, and cortex. The finding that alcohol potentiates the effects of somatostatin, possibly through actions on the G protein, may provide insight into certain aspects of alcohol actions.

Thus evidence is amassing for a specific action of alcohol on the AC second messenger system. Since there is evidence that many different neurotransmitter-receptor complexes are affected by acute administration of alcohol, and because many of these complexes initiate their actions through the AC system, it is possible that alcohol's effects on the AC system will provide important insights into alcohol's diverse actions on the brain.

Monoaminergic Neurotransmitter Systems

Various neurotransmitters such as dopamines (DA), serotonin, and norepinephrine, collectively known as monoaminergic neurotransmitters, have been found to be affected by acute alcohol administration. Levels of these neurotransmitters have been measured in different regions of the rat brain, including the cerebellum, brainstem, striatum, frontal cortex, hippocampus, and hypothalamus and were not found to differ significantly between LS and SS mice (Spuhler et al. 1987). In contrast, a number of studies have demonstrated that the monoaminergic neurotransmitter systems may play a role in mediating alcohol's effects on appetite and reinforcement (Samson et al. 1988).

The DA neurotransmitter system is being studied, and evidence has suggested that in addition to purported roles in various mental and movement disorders, DA may mediate the reinforcing properties of alcohol. Engel and Liljequist (1983) showed that low doses of alcohol had a stimulatory effect on DA neurons. Recently, in a study involving both in vivo and in vitro techniques, Engel and collaborators found that the calcium blocker nifedipine prevented the stimulatory effects of alcohol on both behavior and DA biochemistry, suggesting that enhancement of calcium flux may mediate alcohol's effects on DA neurons (Engel et al. 1988). Reports that alcohol also potentiates DA-stimulated AC activity and that it does so by altering the activities of the regulatory G protein and the AC catalytic unit have been discussed above (Rabin and Molinoff 1981; Luthin and Tabakoff 1984).

In an electrophysiological study, Gessa et al. (1985) demonstrated that alcohol activates the firing rate of brain cells containing DA. DA neurons in certain areas of the brain, specifically those that innervate (supply nerves to) the limbic and prefrontal cortex, were especially vulnerable to alcohol. Alcohol's specificity for altering only certain DA pathways was confirmed and extended by means of a behavioral paradigm in which brain DA levels in specific brain regions were measured in freely moving rats using the transcerebral dialysis technique (Imperato and Di Chiara 1986).

More recently, Fadda et al. (1989) have used selectively bred lines of rats that preferentially drink alcohol solution rather than water (known as Sardinian alcohol-preferring, sP, and non-preferring, sNP) to explore further the mechanism of alcohol's effects on the DA system. They reported that acute alcohol administration resulted in the modification of DA breakdown products and did so to a greater degree in the sP animals. These findings suggested that there may be a genetic basis for alcohol preference that may be related to alcohol's effects on DA neurotransmission.

Studies examining the acute effects of alcohol on serotonin have also proven fruitful. Manipulation of brain serotonin has been found to modify an animal's alcohol consumption (Hill 1974; Melchior and Myers 1976). Substances that act by slowing down the removal of serotonin from its receptor sites, known as "uptake blockers," have been found to reduce the amount of alcohol that animals and humans choose to ingest (Amit et al. 1984; Lawrin et al. 1986; Murphy et al. 1985). In a recent study, P and NP rats were used to explore possible mechanisms underlying alcohol's effects on serotonin-mediated processes (Murphy et al. 1988). The investigators used a behavioral paradigm, comparing voluntary food, water, and alcohol intake in the rat lines before and after a serotonin uptake blocker, fluoxetine, was administered. Fluoxetine, for the most part, only reduced P rats' voluntary alcohol intake as soon as 1 day after treatment. This result suggested that alcohol's effects on serotonin neurotransmission may be different in different genetic lines. The effects of blocking this neurotransmission may be observed acutely (Wong et al. 1985). The implications of this study, that serotonin uptake blockers might be useful for controlling behaviors related to alcohol craving, will be discussed in the section of this chapter on reinforcement.

Neurohormone and Neuropeptide Systems

Neuropeptides and neurohormones are substances that, like the neurotransmitters, affect synaptic transmission and subsequent behavior. Their synthesis and mode of operation, however, are different from the more classic neurotransmitters. At present, the effects of these substances that may themselves act as neurotransmitters or may act by modulating the activity of other neurotransmitters are being investigated (Kaczmarek and Levitan 1987).

One neurohormone, the corticotropin-releasing factor (CRF), appears to be involved in an arousal system, activating the sympathetic and central nervous systems and enhancing the stress response critical for survival (Koob and Bloom 1985). Using a rat operant conflict paradigm, Thatcher-Britton and Koob (1986) reported that low doses of alcohol reversed stress-related behavioral responses of CRF. This finding suggested that one mechanism for the tension-reducing properties of alcohol may involve suppressing the brain's CRF system. In another study that measured changes in locomotor activity, Breese et al. (1984) reported that in a dose-dependent manner, certain depressant and sedating effects of alcohol can be blocked by another neuropeptide, thyrotropin-releasing hormone. Using LS and SS mice, Erwin and Wu (1989) have recently showed that yet another neuropeptide, neurotensin, appears to act differentially in LS and SS mice and may be acting synergistically with alcohol to mediate thermoregulation and spontaneous motor behavior.

Other studies have reported on possible interactions of alcohol with the opioid neuropeptides. Experiments in which rats were given constant infusions of the opiate morphine or injected with either morphine or benzodiazepines showed that morphine selectively led rats to increase their voluntary consumption of alcohol (Hubbell et al. 1988). Studies of alcohol's effects on the brain's neuropeptide systems are providing additional insight into the behavioral responses observed after acute exposure to alcohol. The biochemical mechanisms of the various neuropeptide effects, including how alcohol may alter intracellular levels, rates of synthesis, release, or degradation of neuropeptides, are not yet known.

Alcohol and the Cell Membrane

In addition to recent studies which suggest that the actions of alcohol may be mediated at specific protein receptor and second messenger systems, there is evidence that many of alcohol's actions may be explained by the ability of alcohol molecules to penetrate cell membranes and alter the physical properties of lipid components of the membrane bilayer (Meyer 1901; Chin and Goldstein 1977a; for reviews see Hunt 1985 and USDHHS 1987). Many of the lipid studies have employed higher concentrations of alcohol than those examining alcohol's actions at receptors and coupling enzymes. These studies have focused on the anesthetic-like effects of alcohol, including sedation and changes in temperature regulation, rather than on behaviors that are observed after low doses of alcohol consumption, such as changes in anxiety, locomotor activity, motor coordination, and cognition. Concurrently, the effects of anesthetic doses of alcohol on membrane-bound proteins and channels are being studied (Dolin et al. 1988).

Some of alcohol's effects on the various protein constituents of the cell membrane could possibly be due to indirect action, resulting from alcohol's effects on the lipid bilayer. It has also been suggested that a certain lipid-bilayer fluidity may be necessary for proteins and other enzyme constituents to function optimally. In addition, questions remain unanswered concerning whether alcohol interferes with specific lipid-protein or protein-protein interactions in the membrane or whether alcohol may act similarly to solvents, affecting the membrane-water interface and altering the dielectric constant of the medium (Hoek and Taraschi 1988).

Alcohol molecules may weaken attractive forces between lipid molecules in the cell membrane so that molecules are freer to move within the bilayer. The membrane would thereby lose some rigidity and could become less viscous and more fluid. It has been hypothesized that this "fluidization" may result in the impaired neural processing that occurs with acute intoxication (Chin and Goldstein 1977a). Greater rigidity in the membrane after chronic alcohol exposure might serve as an adaptation to counter the fluidizing effect (Lyon and Goldstein 1983). Physicochemical techniques have been used to demonstrate that cell membranes do have some resistance to alcohol-induced disordering (Rottenberg 1986).

Sensitive methods such as electron paramagnetic resonance (EPR) spectrometry and fluorescence polarization spectrometry have been valuable tools for measuring changes in the physical properties of membranes exposed to alcohol. Studies using these techniques have provided evidence that moderate and high doses of alcohol can increase the fluidity of cell membrane lipids significantly (Harris and Schroeder 1981; Chin and Goldstein 1977a,b). Studies using EPR and fluorescence polarization techniques, however, also have shown that high temperatures alone will produce almost the same kind of membrane-disordering effect as alcohol exposure, without concomitant intoxication (Fraser et al. 1957).

Hitzemann et al. (1986), using the technique of nuclear magnetic resonance, reported that alcohol exerts an ordering effect on the membrane surface and a disordering effect in the membrane interior of rat brain synaptic membranes. The biochemical and biophysical mechanisms for these actions are currently being explored (Boggs 1987; Hoek and Taraschi 1988). Using liposomes (preparations often made from synthetic lipids that can be used as models), researchers have demonstrated that the alcohol-induced disturbance of the lipid bilayer is not dependent on membrane symmetry, lateral inhomogeneity along the membrane, or the presence of membrane components such as proteins or cholesterol (Waring et al. 1981; Taraschi et al. 1985).

Other reports examining alcohol's effects on the lipid properties of membranes in cell culture have been published. Sun et al. (1987) reported that incubation of these cells with high doses of alcohol resulted in enhanced uptake and incorporation of polyunsaturated fatty acids into cell membrane lipids. In cells isolated from rat cerebral cortex, high doses of alcohol inhibited arachidonic acid (a fatty acid) incorporation into phospholipids while enhancing the incorporation into triacylglycerols, thereby changing the constituency of the lipid bilayer (Lin et al. 1988).

An important question is whether there are genetic variations in membrane permeability that could account for individual differences in sensitivity to alcohol. In a study using EPR techniques and membranes from LS and SS mice, Goldstein et al. (1982) reported that membranes from the more alcohol-sensitive LS strain were more sensitive to the fluidizing effects of alcohol than were membranes from the SS line. However, when these studies were repeated using fluorescence polarization, no differences between the two lines were found (Perlman and Goldstein 1984). Because the fluorescent and EPR probes monitor different membrane regions, Perlman and Goldstein suggested that the primary site affected by genetic selection—at least the site that influences sedation in response to alcohol—is localized in a restricted area of the brain cell membrane.

Two developments are likely to influence future research on the effects of alcohol on the membrane's lipid bilayer: one is the discovery that gangliosides (carbohydrate-rich molecules on the surface of cell membranes) may greatly increase the sensitivity of membranes to the disordering effects of alcohol, perhaps by modifying alcohol's ability to penetrate membranes (Harris, Groh, et al. 1984). Another discovery is that membrane alterations associated with tolerance may involve only a subset of membrane lipids including phosphatidylinositol and phosphatidylserine (Taraschi et al. 1986). In addition, it has also been discovered that alcohol can combine chemically with long-chain fatty acids to produce ethyl esters (Laposata and Lange 1986) and that these metabolites of alcohol may be more potent in disordering cell membranes than alcohol itself.

Thus it appears that acute alcohol administration, especially at anesthetic or sedating doses, perturbs lipid constituents of brain cell membranes. Genetic variability in the sedating effects of alcohol has been studied both behaviorally and electrophysiologically, and correlations are indicated between the neuronal excitability of certain brain cell groups and behavioral response to high doses of alcohol. The long-term or chronic effects of alcohol administration on the lipid bilayer, which are discussed in the next section of this chapter, have important consequences for understanding the cellular basis for alcohol tolerance and dependence as well as for understanding alcohol-related disease processes.

Chronic Effects of Alcohol

In order to prevent alcohol abuse and the diseases associated with alcohol dependence, it is important to understand not only the acute actions of alcohol on networks of brain cells but also the changes that occur in the brain with continued alcohol exposure. The underlying question remains: What are the neural and behavioral mechanisms that control and regulate alcohol consumption, which lead some individuals to consume alcohol repeatedly and in quantities that are injurious to themselves or others? To address these issues, investigators are examining the molecular, cellular, and behavioral responses that might perpetuate alcohol drinking.

The processes of tolerance and dependence appear to be critical to understanding chronic alcohol use. Tolerance is the diminished effect of a drug upon repeated administration (Melchior and Tabakoff 1981). It is as if, with chronic use, the brain learns to resist the presence of some alcohol so that a higher dose is required to produce a given effect. Tolerance has been demonstrated in behavioral studies using animals and humans, isolated organs, and even in isolated brain cells. Although alcohol tolerance may enable an individual to maintain higher blood alcohol concentrations (BACs) without appearing intoxicated, the cost of tolerance is that serious tissue damage can develop in the brain, liver, pancreas, heart, and immune system. Tolerance to effects of alcohol is known to occur not only in the brain but also throughout the body, where adaptive changes include an increased rate of alcohol metabolism and the abnormal activation of alternate metabolic pathways (Lieber 1983).

"Physical dependence" is an adaptive state that manifests itself by intense physical disturbances when a drug or alcohol stops being administered, whereas "psychological dependence" has been used to define a condition in which a drug or alcohol produces a craving that requires periodic or continuous administration of the drug to produce pleasure or to avoid discomfort. Koob and Bloom (1988) proposed that both physical and psychological dependence characterize the addicted state and may be inseparable when one attempts to identify the molecular and cellular alterations associated with chronic alcohol use.

A few studies have portrayed the processes of tolerance and dependence after chronic alcohol exposure at the cellular level (Rogers et al. 1979; Chapin and Woodward 1989). For example, in one electrophysiological study of Purkinje cells in the rat cerebellum, it was demonstrated that after 10 to 14 days of alcohol intoxication, the cells stopped responding to the same dose of alcohol (Rogers et al. 1979). When alcohol was withdrawn, Purkinje cell firing was depressed, but when alcohol was re-administered, the depression in cell firing was reversed.

The Mediation and Maintenance of Alcohol Tolerance

In the brain, tolerance appears to be a multifaceted process with both behavioral and cellular antecedents. In a number of studies, tolerance to alcohol has been shown to involve learning. Using approaches in which changes in behavior or physiological response are conditioned through the association of environmental cues with alcohol administration, investigators have shown that some forms of tolerance are dependent on learning (Alkana et al. 1983; Stewart and Eikelboom 1987). For example, the animal might display tolerance only in the environment where the alcohol was initially administered and not in a novel setting (Crowell et al. 1981). Other studies have focused on environmentally independent factors, studying the development of tolerance when alcohol is administered covertly, as part of a liquid diet, or by inhalation techniques (Kalant et al. 1971; Melchior and Tabakoff 1981). Results have also suggested that the factors of dose, duration, and frequency of administration are important for determining the characteristics of alcohol tolerance (Goudie and Demellweek 1986).

In examining the mechanisms of tolerance, investigators have focused on various neurotransmitter, receptor, and second messenger systems that might be involved. The neurotransmitters serotonin and norepinephrine, for example, have been shown to play a role in modulating the acquisition of alcohol tolerance (Grant et al., in press). Le et al. (1981) demonstrated that combined destruction of norepinephrine and serotonin systems completely blocks the development of tolerance to the hypnotic effect of alcohol in the rat. Recently, Szabo et al. (1988) reported that in the mouse, norepinephrine's role in tolerance may depend on its interaction with beta-adrenergic receptors coupled to AC. Experiments in which norepinephrine pathways were chemically obliterated showed that daily injections of forskolin (an activator of AC) would maintain tolerance to the hypnotic effects of alcohol. It is proposed then that norepinephrine and the beta-adrenergic receptor system (which, when stimulated in the presence of alcohol, leads to an increase in intracellular cAMP levels) are important for understanding tolerance. The increase in the intracellular second messenger systems indeed may act to maintain tolerance.

Certain types of calcium channels may be involved in maintaining tolerance to alcohol. When nifedipine, a calcium channel antagonist, was administered to animals that had been chronically exposed to alcohol, acquisition of tolerance was delayed (Wu et al. 1987). It has been demonstrated that in neuronal cell lines, cAMP can induce the production of one type of calcium channel known as dihydroperidine (DHP) sensitive (Miller 1987). On the other hand, calcium channel blockers have been shown to antagonize this type of channel activity. Therefore, cAMP-induced alterations in calcium channel activity in the brain might be important for understanding the mechanisms of tolerance to chronic alcohol use.

The neuropeptide arginine vasopressin (AVP) also has been implicated in the expression and maintenance of alcohol tolerance (Hoffman 1987). AVP is produced in the neurohypophysis, a part of the pituitary gland that has a close fundamental association with the brain. It has been shown that mice tolerant to the hypothermic and hypnotic effects of alcohol remained tolerant after the discontinuation of treatment if they received injections of AVP or one of its analogs (Hoffman et al. 1978; Hung et al. 1984). The maintenance of tolerance by AVP was also demonstrated in paradigms that examined the learned effects of tolerance (Mannix et al. 1986). These studies suggest that AVP may be a factor common to both environment-dependent and environment-independent tolerance and may represent a common underlying mechanism (Grant et al. in press).

Hoffman (1982) suggested that the tolerance-maintaining effect of vasopressin might involve its interaction with specific brain receptors. Indeed, AVP receptors have been identified in the hippocampus and other brain areas that have been associated with learning and memory (Audigier and Barberis 1985; Constantini and Pearlmutter 1984). Szabo et al. (1988) identified one class of AVP receptors, the V1 receptors, as the major site where vasopressin may act to produce tolerance. This finding was established by using agents that bind specifically to V1 receptors. Antagonists to the V1 receptors strongly reduced the ability of vasopressin to maintain alcohol tolerance, whereas the V1 agonists were more effective in maintaining tolerance than vasopressin itself. Another class of vasopressin receptors, the V2 receptors, did not appear to have any role in maintaining tolerance. These findings support the hypothesis that endogenous vasopressin, acting at V1 receptors in the brain, is involved in maintaining tolerance to alcohol. Furthermore, the demonstration that chemical agents can modify the vasopressin-V1 interaction opens the possibility that therapeutic drugs might be developed to modify alcohol tolerance in humans.

The effects of chronic alcohol ingestion on the GABA neurotransmitter system also have been investigated, focusing on changes in metabolism and electrophysiological processes that may reflect alcohol tolerance (Suzdak and Paul 1987). Allan and Harris (1987a) have reported on the chronic effects of alcohol in the brain. Their studies have shown that in neuronal membranes obtained from animals that have been made tolerant to the hypnotic effect of alcohol, the acute stimulatory effect of alcohol on chloride flux is either reduced or absent.

Similarly, many other biochemical systems have been shown to become resistant or tolerant to the effects of alcohol after chronic exposure. For example, whereas the acute effect of alcohol at the NMDA receptor is inhibitory, chronic alcohol ingestion has been shown to result in adaptive changes leading to increased NMDA-mediated responsiveness, an action that would resist alcohol-induced inhibition (Tabakoff et al. in press). The NMDA receptor is said to be "up-regulated" with chronic alcohol administration, a term that refers to its increased sensitivity to agonists. Up-regulation can occur by several mechanisms, including a proliferation of receptor sites or ion channels.

Chronic alcohol exposure also might affect the NMDA receptor system's contribution to memory processes through its effects on long-term potentiation. In acute studies, it was reported that long-term potentiation might be mediated through NMDA receptor-activated calcium flux. In a rat model system, chronic alcohol exposure was found to depress long-term potentiation (Durand and Carlen 1984). In the same report, it was demonstrated that the depression of long-term potentiation was partially reversible following cessation of alcohol intake, a finding that may explain a similar pattern of memory impairment and partial recovery in recently abstinent alcoholics.

In a 1984 study, Harris, Baxter, et al. found that neuronal membranes obtained from animals after chronic exposure to alcohol become resistant to the fluidizing effects of alcohol so that a given dose of alcohol had less effect. Increased membrane rigidity in the chronically treated animals may serve as an adaptive response that has been referred to as membrane tolerance.

In order to further characterize membrane tolerance, biochemical studies were conducted using cell membranes of various organs prepared from animals chronically exposed to alcohol. These studies have demonstrated that membrane tolerance can involve resistance to lipid disordering, a reduced partitioning of hydrophobic molecules into the membrane, and a resistance to the hydrolysis of membrane lipids by exogenous phospholipase A2 (Stubbs et al. 1988; Beauge et al. 1988).

The mechanisms by which adaptive changes occur in membrane lipids after chronic alcohol exposure are being investigated. For example, using a specialized fluorescent collisional quenching technique that enabled direct measurement of various membrane properties, Nie et al. (1989) demonstrated specific alterations in membrane phospholipids that could be responsible for structural modifications in the lipid bilayer in membranes isolated from rats that were chronically exposed to alcohol. Seeking to determine which phospholipids were involved in maintaining membrane tolerance, Hoek and Taraschi (1988) found that in liver membranes, phosphatidyl inositol appeared critical to the process, whereas in brain membrane preparations, phosphatidylserine was required.

In addition to studying the differences between the phospholipids that could account for membrane tolerance, researchers are looking for cellular "triggers" that might control membrane adaptation to alcohol (Aloia et al. 1985; Harris, Baxter, et al. 1984). Recently, evidence has been provided in liver membrane preparations that alcohol's activation of a membrane-bound enzyme called phospholipase C can act on specific components of membrane phospholipids, enabling a cascade of molecular events that may initiate adaptation (Hoek and Taraschi 1988; Gies et al. 1988).

The various changes in membrane phospholipids seen after chronic alcohol exposure are of great interest to alcohol researchers because phospholipids have been shown to be critical to the normal functioning of cells. Phospholipids serve as reservoirs for second messengers such as inositol, triphosphate, and diacylglycerol, and hormone precursors such as arachidonic acid. Moreover, the integrity of phospholipids has been found to be important for membrane proteins to function properly (Majerus et al. 1986).

In summary, tolerance to the effects of alcohol, although a complicated phenomenon, may involve several neural systems such as the AVP and AC systems, and several other neurotransmitter systems such as GABA and NMDA have been shown to modify their activity in response to chronic alcohol exposure. Chronic exposure to alcohol also alters properties of membrane lipid bilayers in the brain.

Alcohol Dependence

The neuronal systems involved in alcohol dependence have proven difficult to pinpoint (Tabakoff and Hoffman 1987), but exploring the processes of alcohol withdrawal has provided some interesting clues to the mechanisms by which alcohol produces dependence. It is known that abrupt withdrawal of alcohol after chronic usage can result in a number of symptoms including severe hangover, profound anxiety, tremulousness, severe sympathetic hyperactivity, sleep disturbances, psychoses, seizures, and even death (Isabell et al. 1955). Some withdrawal signs (e.g., sleep disturbances) can persist for months after cessation of alcohol, a factor that may contribute to relapse. Studies concerning the mechanisms underlying seizure production are proving especially fruitful. Once again, genetically selected lines of animals have been invaluable for such studies and it has been possible to breed mice based on whether they are prone to alcohol withdrawal seizures (WSP) or resistant (WSR) (McSwigan et al. 1984). Changes in lipid fluidity are unlikely to explain this aspect of alcohol dependence because WSP and WSR mice show similar lipid alterations after chronic alcohol exposure (Harris, Crabbe, and McSwigan 1984). In contrast, WSP and WSR mice appear to differ in various brain proteins (Goldman and Crabbe 1986), a finding that has suggested further research into the specific proteins involved in alcohol dependence.

Some investigators have posited a role for GABA-ergic neurons in mediating alcohol dependence and withdrawal phenomena. Currently, there is some debate about whether GABA-mediated chloride flux after chronic alcohol exposure may be important to this process (Morrow et al. 1988; Allan and Harris 1987b). Chronically, alcohol does appear to reduce GABA-mediated inhibition of brain cells. It also has been shown that reducing GABA's inhibition can cause convulsive discharges (that is, seizure activity) in the hippocampus (Miles and Wong 1987). In an attempt to understand the convulsive phenomena, a number of research groups are investigating the long-term regulation of GABA conductance, the GABA receptor, and ion flow (Inoue et al. 1986; Ticku 1987; Stelzer et al. 1988; Ulrichsen et al. 1988). Here, evidence points to the importance of the cAMP system and magnesium ions for the normal maintenance of GABA-ergic activity and the GABAa receptor.

Recently it has been suggested that the alterations in GABA neurotransmission that result from chronic alcohol consumption and that may be causal in the genesis of seizures may be related to the alterations at the NMDA receptor that also have been implicated in seizure activity (Stelzer et al. 1987). In an in vitro study, these investigators stimulated fibers in the hippocampus until they produced NMDA receptor-dependent seizure discharges. Such NMDA stimulation was found to reduce GABA-ergic activity. This may suggest that the modulation of GABA-ergic inhibition by NMDA receptors may underlie certain forms of seizures.

The increased NMDA sensitivity after chronic alcohol exposure could thus contribute to alcohol withdrawal seizures. For example, if chronic alcohol exposure leads to an increase in the number of NMDA receptors, there would be increased sensitivity to glutamate and decreased GABA-ergic activity, and a possible result could be the increased neural excitability that is characteristic of alcohol withdrawal. To test this hypothesis, Tabakoff et al. (in press) conducted a study in which mice that had been chronically exposed to alcohol were withdrawn abruptly. When the NMDA antagonist MK801 was administered, withdrawal seizure severity was reduced in a dose-dependent manner, thus providing evidence in favor of this hypothesis. Because the NMDA receptor is coupled to a calcium channel, one can consider that intracellular calcium levels may be a critical element of cellular excitability and withdrawal seizures. Thus, it is not surprising that changes in other types of calcium channels (e.g., voltage-sensitive calcium channels) also may contribute to alcohol withdrawal seizures.

Chronic alcohol exposure has been shown to result in an increase in voltage-sensitive calcium channels both in cultured cells and in the brain (Messing et al. 1986; Dolin et al. 1987). Investigating the molecular basis for the chronic effects of alcohol on membrane calcium channels using PC12 cells (a clonal cell line derived from brain tissue), Messing et al. (1986) found that acute exposure of the cultured cells to alcohol decreased their uptake of calcium but that prolonged exposure (2-10 days) increased it. The increased calcium uptake after chronic exposure appeared to be an adaptation to alcohol that involved increased activity of the calcium ion channels. Agents such as DHP that block certain voltage-sensitive calcium channels have been shown to reduce signs of alcohol withdrawal in both animals (Dolin et al. 1986) and humans (Koppi et al. 1987). These findings suggest that calcium channel-blocking agents might be designed to improve the management of alcohol withdrawal seizures.

The Role of Second Messenger Systems in Tolerance and Dependence

Chronic alcohol use appears to alter the functions of several neuronal membrane proteins that control the levels of intracellular second messengers (e.g., AC, phospholipase C, and calcium). In neural cell culture studies, Gordon et al. (1986) reported that acute alcohol exposure led to marked increases in receptor-stimulated cAMP levels and that chronically treated cells appeared to become both tolerant to alcohol (requiring more alcohol to maintain normal receptor-stimulated cAMP levels) and dependent on it (showing reduced receptor-stimulated cAMP when alcohol was removed). Bode and Molinoff (1988) found that cultured lymphoma cells exposed acutely to alcohol showed increased activity in the beta-adrenergic receptor-coupled AC system and that chronic exposure reduced activity in the AC system. The same phenomena have been shown to occur in certain brain areas by Valverius et al. (1987).

Diamond et al. (1987) also examined the effects of alcohol on cAMP production in human alcoholics. Their studies have examined changes in cAMP production in lymphocytes, a class of white blood cells that was found to be similar to neurons with respect to the presence of adenosine receptors and the ability of adenosine binding to increase cAMP. In comparing baseline and receptor-stimulated cAMP levels in alcoholics, normal subjects, and patients with nonalcoholic liver disease, the investigators found that lymphocytes from alcoholics showed a marked reduction in both their baseline and receptor-stimulated cAMP levels. The lymphocytes from the alcoholics also could be distinguished from the other groups in that they were remarkably resistant to stimulation of cAMP synthesis by the addition of alcohol to the medium. When lymphocytes from alcoholics and control subjects were grown in cell culture, it was demonstrated that even after 4 to 6 cell divisions, the lymphocytes from alcoholics continued to show abnormalities in cAMP production (Nagy et al. 1988). Another type of cell from the blood of alcoholics was also shown to be less responsive to agents that stimulate AC. Tabakoff et al. (1988) showed that platelet AC activity differences could distinguish between alcoholic and control subjects. Evidence also has been presented to show that the differences are due to altered G protein functions in alcoholics. These groups of investigators are continuing to examine whether the reduced levels of cAMP in cells from alcoholics is due to membrane alterations produced by chronic alcohol or to preexisting and genetically determined membrane differences in alcoholics.

The possibility that changes in the regulation of AC may partly mediate tolerance and dependence is supported by other recent studies that have identified a subunit of the AC-regulating G protein that is strongly affected by chronic alcohol exposure. It is known that selective changes in the function of G proteins in the brain can affect neurotransmission, ion channels (including calcium channels), and cAMP activity (Grant et al. in press). Mochly-Rosen et al. (1988) found that chronic exposure of cultured cells (neuroblastoma-glioma cells) to alcohol impairs the synthesis of the alpha subunit of Gs, the protein that normally stimulates AC activity in the presence of prostaglandin E1 or adenosine. Nhamburo et al. (1988) found evidence that chronic alcohol exposure also alters the properties of the alpha subunit of Gs in cerebral cortical membranes. These reports, showing specific alterations in G proteins, are provocative because they indicate that alcohol exposure can affect gene expression and that alcohol-induced changes in these basic cellular processes may play a role in maintaining tolerance and dependence.

Behavioral Measures and Alcohol as a Reinforcing Substance

Studies examining the behavioral consequences of alcohol consumption are another important focus for alcohol research because these consequences appear to play a major role in determining whether alcohol abuse and dependency will develop. To understand the effects of alcohol consumption that lead individuals to seek repeated exposure to alcohol beverages and to investigate the brain circuits and processes that mediate these behaviors, investigators have been studying the so-called "reinforcing" properties of alcohol. In general, it is known that an individual will tend to repeat a behavior either when it is associated with some pleasant reward, a process known as positive reinforcement, or when it makes something aversive seem less unpleasant, a process known as negative reinforcement.

Research in the area of alcohol reinforcement has shown that alcohol's effects are complex and cannot be explained easily by any one of these types of reinforcement. For example, alcohol's euphoric effects appear to exemplify a case of positive reinforcement, whereas its anxiolytic effects appear to exemplify a case of negative reinforcement. Considerable progress, however, has been made recently in understanding alcohol's positive and negative reinforcing effects and the neurobehavioral correlates. Moreover, with the establishment of genetic lines of rats with a preference for alcohol, a new animal model of alcoholism is emerging. Selectively bred mouse lines also have been developed for studying behavioral activation or depression following alcohol administration. These behavioral and genetic research developments often have been combined with neuropharmacologic techniques to provide important clues about the brain mechanisms responsible for excessive drinking.

Brain Stimulation, Conditioning, and Activity

Research on alcohol reinforcement has included animal studies of oral consumption, intravenous self-administration, and brain stimulation reward. Several previous methods employed to initiate and maintain alcohol drinking in laboratory animals were fraught with technical difficulties. More recently, new procedures have been developed under which animals either consume high concentrations of alcohol or perform operant responses for alcohol reinforcement without being deprived of either food or water (Samson 1987). These procedures involve such techniques as enhancing the alcohol solutions with sweet tastes, combining alcohol with other rewards, giving the animals prior exposure to alcohol, or exposing the animals first to higher alcohol concentrations than those that will be used during the experiments (Samson et al. 1988). These procedures have been shown to produce reliable and substantial BACs. They demonstrate, however, the complexities of establishing alcohol as a reinforcer.

Evidence that alcohol reinforcement arises from its euphoric properties is shown by studies in which animals learn to self-stimulate in response to alcohol, studies known as "brain stimulation reward" (BSR) studies. In these studies, rats typically perform operant responses (e.g., lever pressing) to deliver brief, low levels of electrical current to specific brain areas. This procedure has been used to evaluate the reward properties of other drugs of abuse (e.g., cocaine and heroin). The effects of the electrical stimulation and the drug on the brain are believed to combine to enhance the reward produced by each. Similarly, alcohol has been found recently to either enhance response rates or reduce the amount of electrical current necessary for reward effects (Lewis and Phelps 1987; Bain and Kornetsky 1989; Musgrave et al. 1989).

Further evidence that alcohol reinforcement arises from its rewarding properties is provided by recent human studies. Nonalcoholic volunteers reported experiencing both euphoria as well as mildly pleasant states after consuming moderate doses of alcohol (Lukas and Mendelson 1988; Lukas et al. 1986). These pleasant states were found during the ascending portion of the blood alcohol curve and were associated with increases in the production of adrenocorticotropic hormone (ACTH) as measured in the plasma, as well as the increase in brain electrical activity (specifically alpha activity) as measured by electroencephalograph (EEG)—recording the brain's spontaneous electrical activity by means of noninvasive scalp electrodes placed over specific brain regions. Neither euphoria, ACTH level, nor alpha EEG was associated with the descending portion of the blood alcohol curve. Differentiating responses that occur soon after alcohol is administered (during the ascending limb of the blood alcohol curve) from those that occur during the descending limb may provide insights into the interrelationship of alcohol's effects on the brain, body, and behavior.

In addition, alcohol is believed to have important anxiety-reducing properties. Sober alcoholics frequently report tension and anxiety reduction as a desirable consequence of their drinking, although they often fail to experience these effects after drinking (Nathan and O'Brien 1971). Anxiolytic effects have also been reported in nonalcoholic individuals (Cole and Davis 1975). Research on animals indicates that alcohol does indeed have anxiolytic effects in various conflict tests (Koob et al. 1984). Typically in such tests, alcohol increases the number of punished responses, viz., the extent to which an animal will tolerate punishment in the process of working toward a reward. Considerable interest has been generated by these effects and the role that the GABA-benzodiazepine neurotransmitter receptor may play in them (Suzdak et al. 1986).

In addition to pleasant responses, alcohol given acutely can produce unpleasant effects. Rats given alcohol in conjunction with a novel taste will avoid the novel taste after such experiences (Baker and Cannon 1982). This "conditioned taste aversion" is believed to be the result of the animal's associating the novel taste with the unpleasant internal reactions produced by the alcohol. These responses to alcohol are perhaps important factors in whether certain people drink and in why many animal species avoid all but the lowest concentrations of alcohol (Cannon and Carrell 1987a,b).

Neurotransmitter Systems Studies

Considerable research has been devoted to the role of various neurotransmitter systems in the reinforcing, anxiolytic, stimulant, and depressant effects of alcohol. DA has been shown to be associated with reward and stimulation produced by alcohol. For example, it was reported that blockade of DA receptors interferes with oral self-administration of alcohol in rats (Pfeffer and Samson 1986). Animals given pimozide, a DA receptor blocker, responded like animals who have had the reward removed from the alcohol they drink. Also, DA release has been shown to be increased early after administration of low doses of alcohol in the nucleus accumbens, suggesting that this complex subcortical area of the forebrain may play a role in mediating rewarding events (Imperato and Di Chiara 1986). These investigators also reported that increases in various measures of activity corresponded with increases in DA release. In studies with genetically selected rats, it was demonstrated that preference corresponded with enhanced brain DA activity (Fadda et al. 1989). Other studies have shown that stimulation of DA release in the brain can inhibit the depressant effects of alcohol (Menon et al. 1987).

Serotonin also has been implicated in alcohol reinforcement, albeit in an opposite way. Serotonin reuptake blockers, which increase the activity of alcohol in the neuronal synapse, have been shown to decrease alcohol consumption in laboratory animals and humans (Naranjo et al. 1986). These effects have been observed at doses that do not suppress other behavioral functioning. The effect of serotonin would, therefore, be the opposite of DA in its role in alcohol reinforcement: Increased DA is involved with alcohol reward (increased drinking) and increased serotonin is associated with decreased alcohol reward (decreased drinking). Several recent studies on the neuropharmacologic differences between P and NP rat lines indicate that there are differences in the response of DA, serotonin, and GABA systems. DA levels are higher and serotonin levels are lower in P rats in comparison to NP rats (Wong et al. 1988; Guan and McBride 1988; Murphy et al. 1988).

Other neurotransmitter systems that have been described in previous sections of this chapter, such as the GABA-benzodiazepine receptor, appear to play a role in the anxiolytic and depressant effects of alcohol. In addition, a role for the endogenous opioid systems in alcohol consumption has been described. Administration of morphine (an opioid agonist) and diprenorphine (a mixed agonist-antagonist) has been shown to enhance drinking of sweetened alcohol solutions (Reid et al. 1987). Consistent with these findings, opioid antagonists like naloxone have been shown to reduce alcohol consumption.

Promising behavioral research is proceeding on other neurotransmitter systems as well. For example, recent research has demonstrated interactions between alcohol and nicotine and shown that the effects of nicotine are more potent in LS than in SS mice (de Fiebre and Collins 1988; Burch et al. 1988). These findings implicate the neurotransmitter acetylcholine, and specifically its nicotinic receptor, in behavioral responses to chronic alcohol exposure.

Alcohol Effects on the Human Brain

Although it has long been evident that the human brain is very susceptible to the acute and chronic effects of alcohol, the nature of these effects has been difficult to study in living human subjects. The accessibility of the human brain for study has been greatly improved with new computer-aided technologies to "image," or view, brain structures and to record brain activity. The brain scanning techniques that are commonly used by alcohol researchers, including scanning by computerized tomography (CT) and magnetic resonance imaging (MRI), provide high-quality static pictures of brain structures. Other imaging technologies, such as PET and cerebral blood flow (CBF), provide alcohol researchers with more dynamic images. In these dynamic studies, slices through the brain are recorded over a period of time while radioactive-labeled tracing compounds highlight the brain's use of oxygen or essential nutrients.

To examine brain activity, alcohol researchers have been using electrophysiological techniques. Electrophysiological measures of brain activity have been found to be quite sensitive to various alcohol effects, including intoxication, tolerance, withdrawal, and long-term brain dysfunction. Capitalizing on the close association between the brain's bioelectrical and chemical states of activity, electrophysiological recordings can provide dynamic representations of brain function that may be used to detect brain abnormalities even when no abnormalities are evident on CT scans.

The correlation of acute and chronic alcohol use with specific impairments in cognitive and psychological functions is also being explored by alcohol researchers. In particular, recent studies have been examining the association between chronic alcohol abuse, loss of brain tissue, and various neuropsychological impairments. Neuropsychological studies typically measure capacities such as language, memory, reasoning, perception, and other cognitive processes.

Psychological factors associated with alcoholism such as depression, anxiety, and aggression are also being explored. Recent advances in understanding the functional, structural, and neurobehavioral consequences of alcohol use will be considered in turn.

Electrophysiological Studies

Using EEG technology (see fig. 6), investigators have demonstrated that alcoholics as well as first-degree relatives of alcoholics who do not abuse alcohol, including 12-year-old sons of alcoholics, can show specific differences from controls in specific brain wave patterns (Gabrielli et al. 1982). In addition, it has been demonstrated that the EEGs of sons of alcoholics reflect greater sensitivity to challenge doses of alcohol than do those of control subjects (Pollock et al. 1983). These studies are intriguing because they suggest that alterations in the brain's electrical activity might be apparent not only in alcoholics but also in individuals at risk for developing alcohol abuse and dependence. Also, these studies provide evidence that certain measures of brain activity might serve as biological markers for predisposition toward alcoholism (see chapter III).

Many recent studies have used the technique of event-related potentials (ERP) to explore the alterations in the brain's electrical activity. ERP

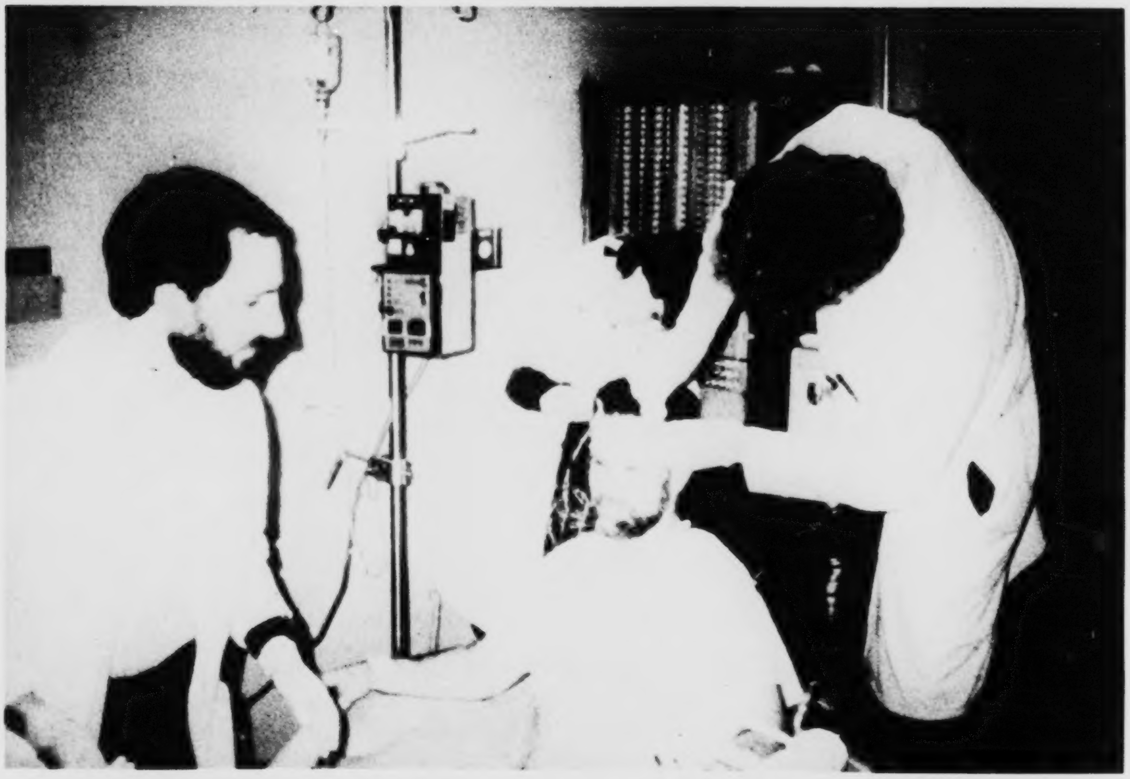


FIGURE 6. Electrodes are placed over specific brain regions on an NIAAA intramural research program control subject. Provided by Dr. Boris Tabakoff.

is a technique in which electrical potentials are recorded noninvasively in response to discrete visual, auditory, or sensory stimuli. These potentials are presumed to reflect stages of the brain's information processing as they occur in various brain circuits. For example, it has been found that when subjects are required to discriminate between stimuli, there is usually a large positive brain wave that occurs approximately 300 milliseconds after the stimulus presentation, which is referred to as the P3 (or P300) wave. It has been proposed that the neural generator for P3 may originate in the hippocampus, an area of the brain that has been implicated in various memory functions (Halgren et al. 1980; Johnson et al. 1985). To assess differences between individuals' ERP brain waves, investigators use stimuli that challenge one of the sensory systems (e.g., vision or audition) and measure whether there are delays in the latency to initiate the expected responses and/or whether there are changes in the amplitude (size) of the responses. It is interesting that latency, amplitude, and other parameters of P3 waves have been reported to be highly similar between identical twins and siblings (Polich and Burns 1987; Steinhauer et al. 1987). This similarity suggests a genetic basis for the P3 response.

Studies that have recorded ERPs in abstinent alcoholics while attempting to discriminate between visual stimuli also have reported delays in the P3 response relative to nonalcoholic control subjects (Porjesz et al. 1987a; Hill et al. 1988). Other ERP responses such as the N2 component, a negative potential occurring approximately 200 milliseconds after a stimulus is presented, similarly have been found to be affected by chronic alcohol use (Porjesz et al. 1987b). Studies demonstrating that even in abstinent alcoholics there is a delay in the transmission of information reveal that there are long-term effects of chronic alcohol use. When properties of the visual stimuli are manipulated, e.g., by changing their motivational relevance or their probability of occurrence, abstinent alcoholics were found to display a unique deficit in the amplitude of the P3 response but not in its latency (Porjesz et al. 1987a). Together, these ERP studies suggest that alcoholics have multiple deficits in processing information and that these may be mediated by multiple brain circuits.

In addition to studies that have demonstrated ERP impairments in alcoholics, a number of investigators have recorded ERPs in subjects at risk for alcoholism (see fig. 7). Some studies using visual stimuli have found that offspring of alcoholic fathers display P3 abnormalities, especially when the tasks are particularly complex (Elmasian et al. 1982; Begleiter et al. 1984; O'Connor et al. 1987). In one recent study requiring offspring of alcoholics and control subjects to make an auditory discrimination as accurately as possible (rather than stressing the speed of response), Begleiter et al. (1987) reported another P3 anomaly. They found that the rise time of the P3 wave was decreased in at-risk boys relative to their peers (Whipple et al. 1988). In contrast, some studies that have used less complex auditory (Polich, Burns, and Bloom 1988) or visual (Polich, Haier, et al. 1988) discrimination tasks have shown that P3 brain waves from youths with a family history of alcoholism could not be discriminated from those of youths with no such family history. (For more discussion of the P3 amplitude, see chapter III.)

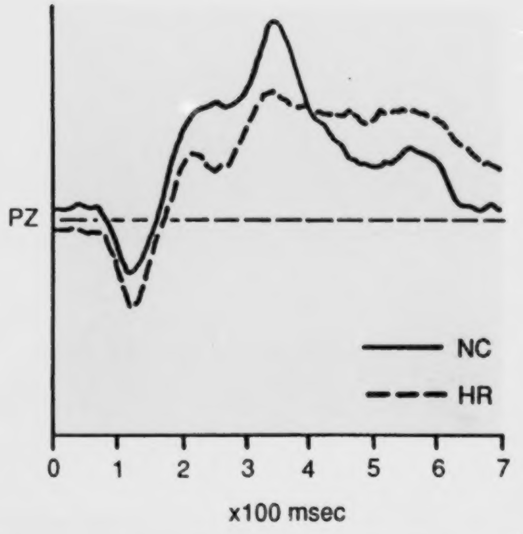


FIGURE 7. Event-related brain potentials from a normal control subject (NC) and from a subject at high risk for alcoholism (HR). Peak amplitude is shown to be reduced in the P3 brain wave of subjects at high risk.
Provided by Dr. Henri Begleiter.

Brain Imaging Studies

Tarter and Edwards (1986) pointed out that the relationship between chronic alcohol use and brain anatomical and functional changes is complex and involves many factors. For example, age and health status can affect brain structure just as factors such as premorbid intelligence can affect neuropsychological performance, either exacerbating or mitigating the effects of alcohol consumption. In addition, it is important to consider that some factors that have been associated with the loss of brain tissue (i.e., atrophy) such as head trauma, malnutrition, and liver disease, although commonly associated with chronic alcohol use, also can occur independent of alcohol use. For example, in one recent study, Tarter et al. (1988) demonstrated that many of the brain impairments that are observed in chronic alcoholics are observed in patients with liver disease who have no history of alcoholism.

CT studies of the alcoholic brain have consistently demonstrated brain atrophy (Ron 1983; Wilkinson 1982). Although the findings from different studies vary in some details, chronic alcohol use in general has been associated with loss of brain weight, increased spaces (called "sulci") between the convolutions on the brain's cortical surface, and enlargement of the cerebral ventricles (cavities in the brain that are usually filled with a tightly regulated amount of the blood filtrate known as cerebrospinal fluid).

The most recent CT investigations have been applying quantitative and statistical techniques to the analysis of brain images and controlling for the effects of age and health status that might otherwise confound data. In one such study, Pfefferbaum et al. (1988) demonstrated that alcoholics had larger ventricles and less brain tissue than controls; that enlargement of the ventricles was not apparent in younger alcoholics but became more prominent in older patients; that enlargement of the sulci was present among alcoholics of all ages; and that enlargement of both the sulci and the ventricles was correlated with the total amount of alcohol consumed over the patients' lifetime (see fig. 8). From their data, the investigators suggested that finding enlarged sulci even in young alcoholics implies that the cortex may be less resilient than other areas of the brain to the effects of alcohol and may degenerate first. Another interesting possibility is that some brain atrophy may precede excessive alcohol consumption. By contrast, the ventricles, which are affected by multiple factors including nutritional

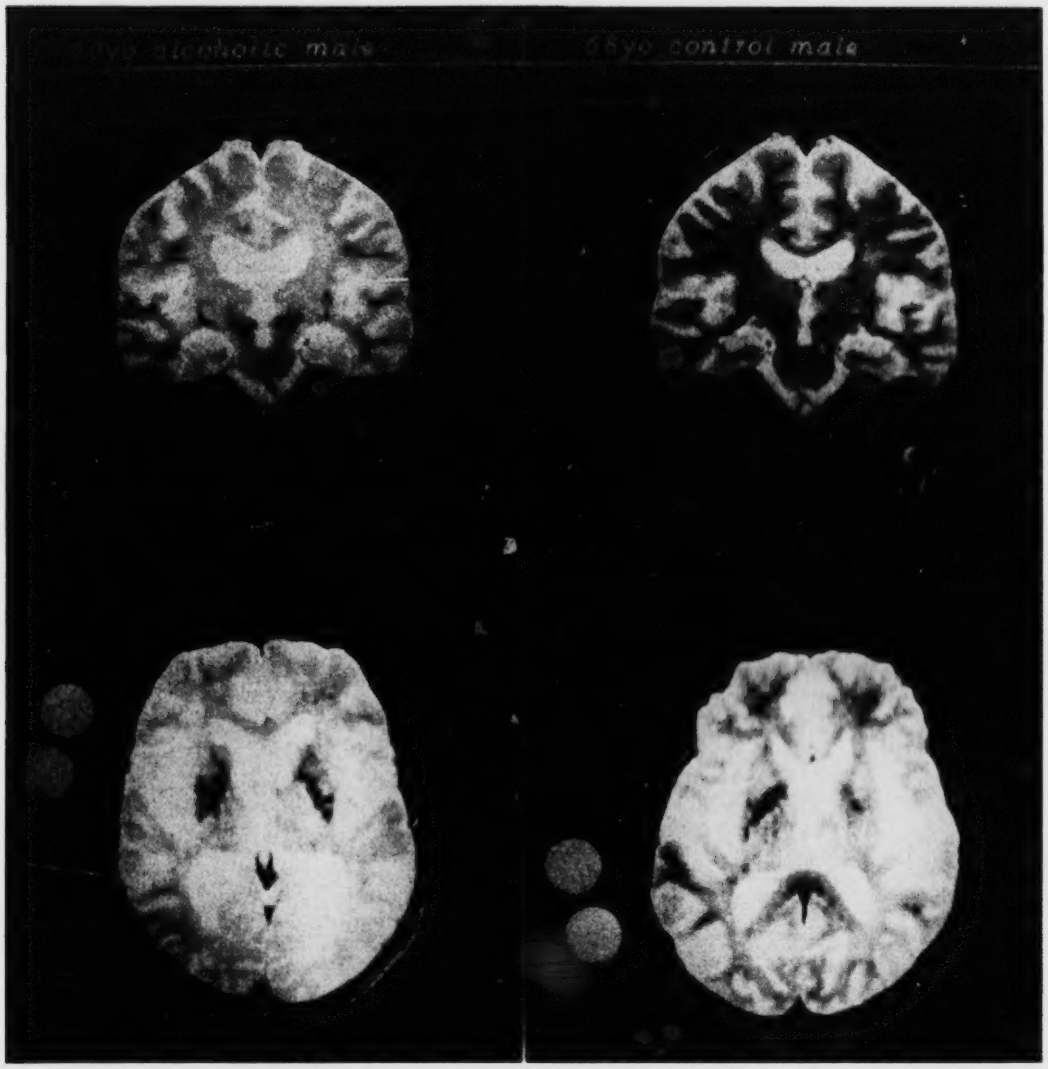


FIGURE 8. Brain images of 60-year-old alcoholic and 68-year-old control.
Provided by Dr. Adolf Pfefferbaum.

status, appear to become increasingly vulnerable to the effects of alcohol with increasing age. In related research investigating the effects of alcohol on cells from a structurally simpler area of cortex, the hippocampus, Niesen et al. (1988) reported electrophysiological changes in cells from old rats that were not apparent in younger rats.

Recent studies using MRI imaging have examined the brain atrophy associated with Wernicke's encephalopathy (Charness and DeLaPaz 1987). Before the development of MRI imaging, Wernicke's encephalopathy (one of the complications of chronic alcohol use caused by a nutritional deficit of the vitamin thiamine) often went undiagnosed unless patients were autopsied after death. By quantitative examination of MRI brain images in patients with Wernicke's disease and control populations, Charness et al. (1988) demonstrated that in addition to ventricular enlargement, and independent from age effects, this group of alcoholic patients had a unique loss of tissue in the area of the brain known as the mamillary bodies. This finding is provocative because lesions of the mamillary

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bodies have been associated with the types of cognitive and short-term memory dysfunction that are often observed in alcoholic patients. (For more discussion of Wernicke's disease, see chapter V.)

Preliminary studies using PET and CBF also have been conducted to investigate brain pathophysiology in alcoholic patients (Chao and Foudin 1986; Eckardt, Rohrbaugh, et al. 1988) (see fig. 8). One PET study found that when compared with age-matched control subjects, long-term abstinent alcoholics with documented memory impairments underused glucose, the brain's primary source of energy. In examining which brain regions were responsible for this decrement, it was found that some patients, specifically those who displayed more clinical dementia, showed lower glucose use in the frontal areas of cortex, whereas other patients underused glucose more in subcortical areas such as the thalamus and basal ganglia. In many other neurological and cognitive function studies, a similar dissociation between cortical and subcortical dementias has been used to model the different dementing illnesses. CBF studies have shown that in alcoholics who have been medicated, there are also specific decrements in blood flow that can be correlated with the magnitude of chronic alcohol use (Samson et al. 1986; Risberg and Bergland 1987). Further research in this exciting new area should provide insight not only into the consequences of chronic alcohol use but also into the brain circuits and mechanisms responsible for producing motor and cognitive capacities.

Neuropsychological Studies

In alcoholics, the assessment of neuropsychological capacities has proven useful for differential diagnosis, monitoring improved cognition with abstinence, and placing patients in appropriate treatment programs (Eckardt, Rawlings, et al. 1988). Neuropsychological assessment has also been shown to predict posttreatment employment status (Donovan et al. 1984). In addition, studies that are able to characterize specific neuropsychological deficits in alcoholics are useful to other brain scientists investigating brain/behavior relationships and modeling complex brain functions such as memory.

The issue of whether there are measurable alcohol-related cognitive impairments among nonalcoholic social drinkers appears unresolved at present (Parsons 1986). The most recent studies suggest, however, that experimental variables such as subject selection, determination of drinking status, and the particular neuropsychological tests used to measure cognition might bias test results. In a well-controlled study, Emmerson et al. (1988) reported no dose-dependent correlation between alcohol consumption and cognitive performance.

Alcoholics without clinically apparent neurological impairments had been thought to exhibit a characteristic profile of impaired cognitive functions. In general, a number of studies had reported a pattern of deficits in this group of alcoholics, involving deficiencies in abstract thinking and visuospatial problem solving with relatively intact memory functions (Parsons and Farr 1981). To some investigators, these studies suggested that deficits in abstraction and visuospatial problem solving might represent the earliest manifestations of general cognitive decline. Other investigators have suggested that memory problems might occur in a separate subgroup of alcoholics or that memory functions indeed may be compromised when tested appropriately. To explore the memory deficits that are observed in alcoholics, the most recent studies have attempted to apply new theoretical models, which propose that memory is controlled and regulated by multiple systems that may be located in different brain circuits (Wilkinson and Poulos 1987; Salmon and Butters 1987; Oscar-Berman and Ellis 1987; Riege 1987; Lister et al. 1987).

In alcoholics who have entered treatment programs and been given neuropsychological tests, it has been reported that 45 percent to 70 percent show specific deficits in problem solving, abstract thinking, concept shifting, psychomotor performance, and difficult memory tasks (Parsons and Leber 1981; Eckardt and Martin 1986; Tabakoff and Petersen 1988). In the most severe alcoholics, serious organic cerebral impairment is a common complication, occurring in about 10 percent of the patients (Horvath 1975).

The diverse signs of severe brain dysfunction that persist after cessation of alcohol consumption have been conceptualized in terms of two organic mental disorders: alcohol amnestic disorder, which is commonly referred to as Korsakoff's psychosis or Wernicke-Korsakoff syndrome, and dementia associated with alcoholism (Martin et al. 1986; Lishman et al. 1987). The alcohol amnestic disorder is characterized by short-term memory impairments and behavioral changes that occur without clouding of consciousness or general loss of intellectual abilities.

Dementia associated with alcoholism consists of a global loss of intellectual abilities and impairment in memory function together with disturbances of abstract thinking, judgment, other higher cortical functions, or personality change without a clouding of consciousness. It has been suggested that subcortical lesions that may result from nutritional (e.g., thiamine) deficits are characteristic of Korsakoff's, whereas alcoholic dementia is associated with cortical changes (Victor and Laureno 1978; also see chapter V).

The question of whether alcoholics are aware of their neuropsychological impairments also has been addressed recently (Shelton and Parsons 1987). The investigators found that compared with age-matched controls, alcoholics did report having more problems with memory, language skills, and perceptual-motor functions and did perform more poorly than control subjects; however, there did not appear to be a correlation between the degrees of perceived and measured impairment.

Research is proceeding to discover whether the cognitive impairments in alcoholics are reversible in those who abstain. Goldman (1986, 1987) reported apparent spontaneous recovery of cognitive function among abstinent alcoholics, a result that may be due solely to the absence of alcohol but that also may be due to other changes such as better nutrition and opportunities for social interaction. There are also reports that cognitive training with remedial mental exercises can facilitate recovery from impairment.

In addition, CBF studies have demonstrated improvements in blood flow with abstinence and treatment (Meyer et al. 1985; Ishikawa et al. 1986). Recently, Muuronen et al. (1989) reported results from a longitudinal study in which a group of alcoholic patients who had received CT scans and neuropsychological tests were retested after 5 years. Those patients who had been abstinent had less brain atrophy—both cortical and subcortical—after 5 years than they had at first, although they had more brain atrophy than did subjects in an age-matched control group. The group of abstinent alcoholics showed significant improvements in visuospatial functioning and some small improvement in tests of reasoning and memory.

The reversibility of mental impairment not only might have an impact on the ability of alcoholics to participate in treatment programs but also may provide encouragement for alcoholics to seek treatment. In addition, understanding the specific neuropsychological deficits associated with chronic alcohol use has immediate consequences for treatment programs; that is, patients may benefit more from intervention programs in which there is consideration of the patient's changing cognitive state during the course of treatment (NIAAA 1989).

Alcohol and Aggressive Behavior

In both animal and human studies, alcohol, more than any other drug, has been linked with a high incidence of violence and aggression (Brain 1986; Miczek 1987). Recent studies have associated acute or chronic alcohol consumption with high rates of homicides, suicides, and sexual assaults (Abel and Zeidenberg 1985; Leonard et al. 1985). Sociological studies have examined the contribution of situational, social, and personality factors to aggressive behavior (e.g., Cherek et al. 1985), and genetic studies have reported on the association of aggressive behavior, antisocial personality, and predisposition to alcoholism in individuals at risk (Cloninger 1987). As noted by Winslow and Miczek (1985), the effects of alcohol on aggressive behavior also appear to depend greatly on such factors as drinking context, culture, sex, alcohol dose, and experience.

Recent studies in the neurosciences have focused on the possible contribution of alterations in serotonin levels to aggressive behavior. In animals studies, serotonin has been found to play a role in the regulation of aggression (Eichelman 1979). In human studies, there also have been reports linking low levels of a metabolite of serotonin, 5-HIAA, with aggressive and suicidal behaviors (reviewed by Asberg 1986). Regarding alcohol's association with aggressive behavior, it has been reported that relatively high percentages of alcoholics attempt and commit suicide and that alcoholics have lower levels of serotonin than age-matched controls (Roy et al. 1987). Linnoila et al. (1983) also reported that male murderers and attempted murderers have lower levels of 5-HIAA in their cerebrospinal fluid than controls. In one study, impulsive offenders who had at some time attempted suicide were found to have significantly lower 5-HIAA levels than violent offenders who had never attempted suicide. Results from these and other related studies led Roy et al. (1987) to suggest that there may be a subgroup of alcoholics who have a defect in their central serotonin system. These individuals may start to abuse alcohol at an early age and may manifest an antisocial personality disorder and impulsive violent behavior toward themselves and others.

It is noteworthy that dominance and submissiveness in monkey groups also have been found to be associated with neurochemical and endocrine factors. For example, serotonin and its metabolite 5-HIAA are found at higher levels in dominant monkeys than in submissive ones (Raleigh et al. 1983). High testosterone levels, as well, have been consistently associated with dominance in several species of monkeys (Rose et al. 1971; Bernstein et al. 1983; Steklis et al. 1982; Coe et al. 1983).

The possibility of a link between testosterone levels and the ability of alcohol to increase aggression was strengthened in a recent study by Winslow et al. (1988) in which the interactions between alcohol, testosterone levels, and aggressive behavior were examined in squirrel monkeys. Administering testosterone for several weeks caused no increase in the baseline aggressiveness of dominant monkeys, although their aggressiveness was increased by low doses of alcohol. Submissive monkeys similarly treated with testosterone, however, did become aggressive when given low doses of alcohol. Because a previous study from the same laboratory (Winslow and Miczek 1985) had shown that alcohol alone at any dose did not trigger aggressiveness in the submissive monkeys, it is likely that testosterone administration in the recent study mediated this effect. These findings suggest that testosterone may activate alcohol-sensitive brain mechanisms involved in aggressive behavior.

Summary

Neuroscience research on alcohol abuse and dependency is progressing rapidly with investigations attempting to uncover the molecular, cellular, and behavioral bases for alcohol's actions on the brain. In particular, there is sufficient evidence that doses of alcohol that are typical of those commonly consumed affect specific proteins along brain cell membranes. This finding is in contrast with previous research based on studies that used higher doses of alcohol, which concluded that alcohol acts as a general membrane perturbant, affecting the brain primarily by altering the membrane lipid bilayer.

The proteins that have been of interest to alcohol researchers are involved in the function of a number of neurotransmitters, such as GABA, glycine, and glutamate, particularly with its NMDA receptor. Research on the NMDA receptor has been especially encouraging because a number of activities regulated or controlled at this receptor are known to be altered by alcohol consumption, including memory, seizure threshold, and cell growth during fetal development. Other proteins that have been of interest to alcohol researchers are those that control the opening and closing of ion channels; recent studies have demonstrated how chloride and calcium channels in particular are affected by alcohol use. It has long been established that substances that affect the normal flow of these ions across the cell membrane to even a small degree can seriously compromise brain cell activity.

In addition, studies have demonstrated that both acute and chronic administration of alcohol alters the activities of second messenger systems. The activities of the second messengers are fundamental to cellular well-being. The effects of alcohol on one such second messenger system, the AC system, have received much attention because it has been found that one of the AC system's subunits, the G protein subunit, is especially vulnerable to alcohol.

Chronic alcohol use can lead to the states of tolerance and dependence. Alcohol researchers have found that certain neurohormones such as vasopressin may play a critical role in maintaining tolerance and that other neurotransmitters, receptors, and ions such as calcium may play a role in mediating tolerance to alcohol. Once again, the chronic effects of alcohol on the activity of the second messenger AC have provided a lead toward uncovering the mechanisms underlying these states.

Tolerance to the effects of alcohol, although a complicated phenomenon, is being unraveled by alcohol investigators. Several neural systems, such as the AVP and AC systems, have been shown to play a role in mediating and maintaining tolerance, and several other neurotransmitter systems such as GABA and NMDA have been shown to modify their activity in response to chronic alcohol exposure. Chronic exposure to alcohol also alters properties of membrane lipid bilayers in the brain as well as in other tissues that may significantly change a host of lipid and protein-regulated functions.

Learned responses to alcohol (i.e., alcohol acting as a reinforcing stimulus) can act to perpetuate drinking behavior in some individuals. Genetically bred rodent lines have been developed that show alcohol preference and that may serve as an animal model for alcoholism.

Studies investigating the effects of alcohol on the human brain have been made possible because of new noninvasive techniques for recording brain activity such as ERP, CT scanning, PET, and CBF studies. Electrophysiological studies (EEG recordings) have shown that sons of alcoholics have greater sensitivity to challenge doses of alcohol than controls do. These studies are intriguing because they suggest that alterations in the brain's electrical activity might serve as biological markers for predisposition toward alcoholism. Measurement of the P3 brain wave (a brain wave that occurs in certain cognitive functions) has shown that nondrinking offspring of alcoholic fathers display P3 abnormalities. Further research will be necessary to characterize the specific alterations in the brain's electrical activity that might predispose some individuals to alcoholism.

In conjunction with those studies, neuropsychological studies have been able to document that there can be some reversal of the cognitive losses and structural damage in those alcoholics who abstain from drink. Together, the basic animal studies and the clinical research have pointed the way for exciting breakthroughs in the next decade of neuroscience research on alcoholism.

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Chapter V

Medical Consequences

Introduction

Alcohol affects almost every organ system in the body either directly or indirectly. However, there are differing levels of susceptibility to medical consequences of alcohol consumption. Some people may be more predisposed, for either genetic or other reasons, to develop adverse medical consequences from alcohol use. Moreover, there appear to be relationships between amount, duration, and pattern (sporadic vs. continuous) of alcohol consumption and the development of medical consequences, although these relationships at present are not completely clear. In addition, factors other than alcohol consumption itself can contribute to the adverse effects of heavy alcohol use.

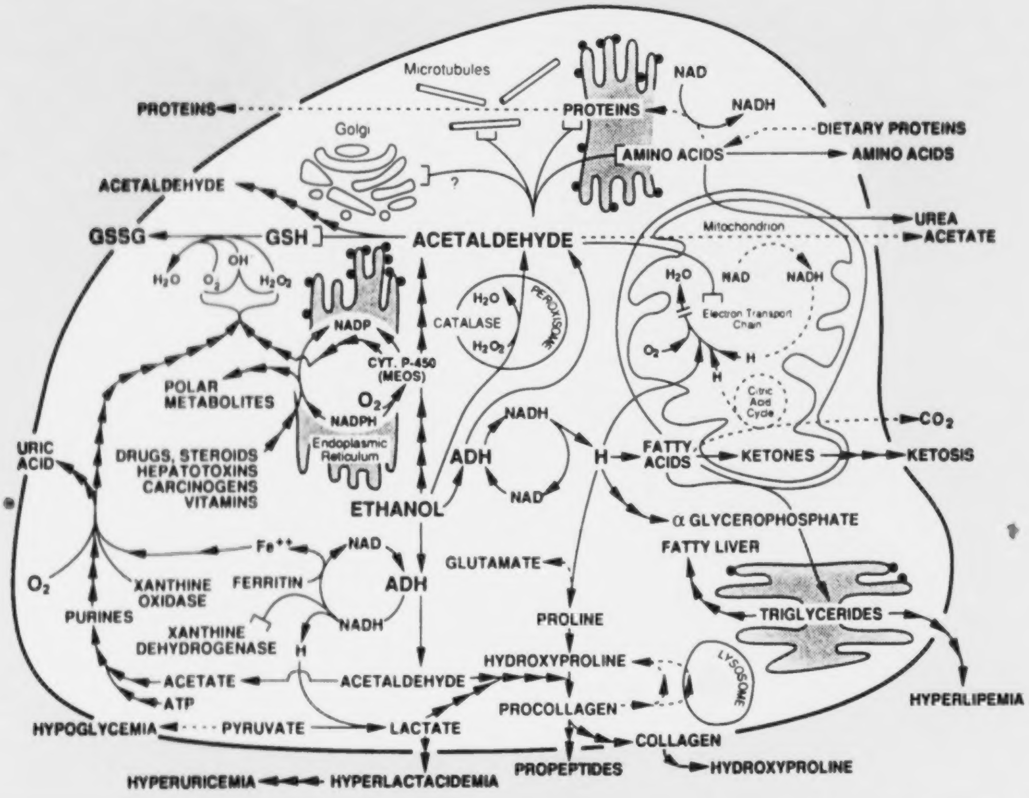
Alcohol-Induced Liver Disorders

The liver, the primary site of alcohol metabolism, can be severely affected by heavy alcohol use (see fig. 1).

Alcohol-induced liver damage is grouped under three major headings: (1) fatty liver, (2) alcoholic hepatitis, and (3) cirrhosis. Histologic evidence of all three can be found simultaneously in the same patient (Maddrey 1988). These disorders were once thought to be invariably progressive stages of alcohol-induced liver injury, but the results from human and animal studies now suggest that cirrhosis may develop in the absence of any evidence of prior hepatitis (Lieber 1984a; Maddrey 1988; Popper and Lieber 1980).

The three types of alcohol-induced liver disorders differ in their prognoses: Fatty liver and alcoholic hepatitis are reversible with abstinence, whereas cirrhosis is not. They also differ in estimates of their incidence: Among heavy drinkers, 90 to 100 percent show evidence of some features of fatty liver, an estimated 10 to 35 percent develop alcoholic hepatitis, and 10 to 20 percent develop cirrhosis (Grant et al. 1988). However, it has been estimated from autopsy studies that 40 percent of cirrhosis is not detected during life (Lieber 1982).

Mortality from chronic liver disease and cirrhosis (International Classification of Diseases, 9th revision, code no. 571, subsequently referred to as "cirrhosis") has been declining steadily in the United States since 1973. However, in 1986, cirrhosis was ranked as the ninth leading cause of death in this country (NIAAA 1989). Furthermore, an examination of changes in cirrhosis death rates in 29 countries between 1974 and 1983 has revealed significant declines in cirrhosis mortality in Austria, Canada, France, Greece, Hong Kong, Switzerland, and New Zealand, with France showing the greatest decline (Smart 1988;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POLAR METABOLITES
O_2
Citric Acid Cycle
NADPH
NADH
CO_2
Endoplasmic Reticulum
URIC ACID
DRUGS, STEROIDS
HEPATOTOXINS
CARCINOGENS
VITAMINS
ADH
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FATTY ACIDS
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KETOSIS
NAD
ETHANOL
α GLYCEROPHOSPHATE
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NAD
FATTY LIVER
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O_2
XANTHINE OXIDASE
FERRITIN
ADH
PURINES
NADH
PROLINE
TRIGLYCERIDES
XANTHINE DEHYDROGENASE
H
HYDROXYPROLINE
LYSOSOME
ACETATE
ACETALDEHYDE
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PROCOLLAGEN
HYPERLIPEMIA
HYPOGLYCEMIA
PYRUVATE
LACTATE
COLLAGEN
PROPEPTIDES
HYDROXYPROLINE
HYPERURICEMIA
HYPERLACTACIDEMIA

FIGURE 1. Mechanisms of liver injury induced by ethanol (ethyl alcohol, the intoxicating ingredient in alcoholic beverages).
SOURCE: Lieber in press.

Mann, Smart, and Anglin 1988). In 16 other countries, the death rates were lower in 1983 than in 1974 but the changes were not statistically significant.

The downward trend in cirrhosis mortality in the United States and Canada between 1973 and 1984 is difficult to explain, in view of the fact that per capita consumption of alcohol increased in the United States until 1980 and remained relatively unchanged in Canada during the decade in question. Some suggested reasons for the declines in cirrhosis mortality are changes in patterns of consumption, earlier diagnosis and treatment, increases in the proportion of alcoholics receiving treatment, improved medical management, health promotion efforts, and effective prevention programs (Mann, Smart, and Anglin 1988; Mann, Smart, Anglin, and Rush 1988; Smart and Mann 1987).

Other factors in the decline in mortality could have been decreases in cirrhosis from causes other than alcohol, or changes in diagnostic criteria for classifying and reporting cirrhosis deaths following the implementation of the Ninth Revision of the *International Classification of Diseases* (ICD-9) (see fig. 2) (NIAAA 1989). There is some evidence that misdiagnoses on death certificates may account for substantial underreporting of cirrhosis deaths. In a study of patients with biopsied alcoholic liver disease who died during a 10-year followup, Blake et al. (1988) found that ICD-9 diagnoses on death certificates had a 47-percent chance of missing the correct diagnosis of cirrhosis.

Cirrhosis death rates for males have been consistently higher than rates for females; in 1986, the male cirrhosis mortality rate was more than twice the rate for females (NIAAA 1989). However, women appear to have greater susceptibility to alcohol-related liver damage. They develop severe liver disease with shorter durations of alcohol use and lower levels of consumption

(Grant et al. 1988). Further, surveys have shown a higher prevalence and greater severity of alcohol-related liver disease in alcohol-dependent females than in alcohol-dependent males. The reasons for the apparent sex differences in alcohol sensitivity are unknown. They could be related to differences in hormones, immune systems, body weight, or body water content (Grant et al. 1988).

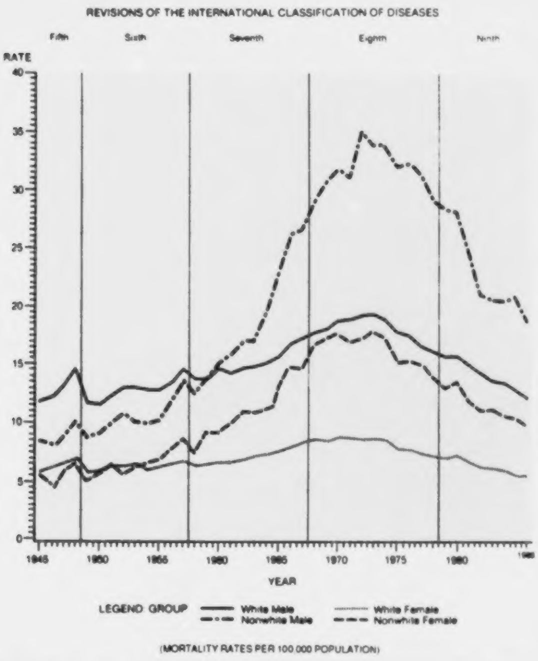

FIGURE 2. Age-adjusted mortality rates from liver cirrhosis by race and sex, United States, 1945–1986.
SOURCE: NIAAA 1989.

The cirrhosis mortality rate for whites was consistently higher than for nonwhites from 1937 through 1956. Beginning in 1957, the nonwhite cirrhosis mortality rate rose sharply, peaking at 25.3 deaths per 100,000 in 1972—nearly twice the rate for whites. In national mortality statistics, Hispanics are categorized as white, and blacks comprise approximately 92 percent of the nonwhite population. Data on nonwhites, therefore, are considered reasonably representative of the black population.

Striking changes have occurred over time in cirrhosis mortality rates for nonwhite males. For this group, cirrhosis death rates were consistently lower than those for white males from 1933 until 1960, when rates for nonwhite males began a steep rise (see fig. 2). By 1969, the rate for nonwhite males was double the 1960 rate. In 1972, nonwhite male mortality peaked at 35 deaths per 100,000 and has declined rapidly since then. The mortality rate for nonwhite females followed a similar pattern, rising steadily above the white female rate from the mid-1950s until 1973, when it peaked at more than twice the rate for white females. However, in the 65-and-over age group, white males and females consistently have higher respective cirrhosis mortality rates than nonwhite males and females (NIAAA 1989).

Seeking explanations for the changing trends in nonwhite cirrhosis mortality rates, Herd (1985) examined migration patterns in the black population. She suggested that social and demographic changes brought about by the mass migration of blacks from the rural South to the urban North were accompanied by increasing levels of alcohol consumption and alcohol-related problems in a population that in earlier decades had been relatively alcohol abstinent.

The amount and duration of excessive alcohol use that lead to liver injury are uncertain. Research (Rubin and Lieber 1968) has shown that it is possible to induce fat accumulation and ultrastructural changes in the liver in young, nonalcoholic volunteers in about a week by substituting alcohol for carbohydrates in the diet in amounts well below those needed to induce intoxication. However, there are marked individual differences in susceptibility to alcohol-induced liver disease (Maddrey 1988) as well as international differences in the relationship between per capita alcohol consumption and cirrhosis mortality rates (see fig. 3). Increased risk of fatty liver has been found at consumption levels greater than 80 grams a day in men and 20 grams a day in women (Grant et al. 1988). Several studies, but not all (Soronson et al. 1984), have found that the severity of liver damage increases with increasing daily intake of alcohol to more than 180 grams per day (approximately 14 standard drinks) when duration of use ranges from 10 to 20 years (Grant et al. 1988). Lelbach (1974) showed that for an individual consuming about 210 grams of ethanol daily for 22 years, the probability of developing cirrhosis is 50 percent, and that it increases to 80 percent after 33 years of similar daily consumption.

Furthermore, genetic factors may affect susceptibility to these disorders; identical twins show some concordance for cirrhosis (Hrubec and Omenn 1981), yet no genetic markers have been found. However, in a recent study a specific pattern associated with a gene coding for type 1

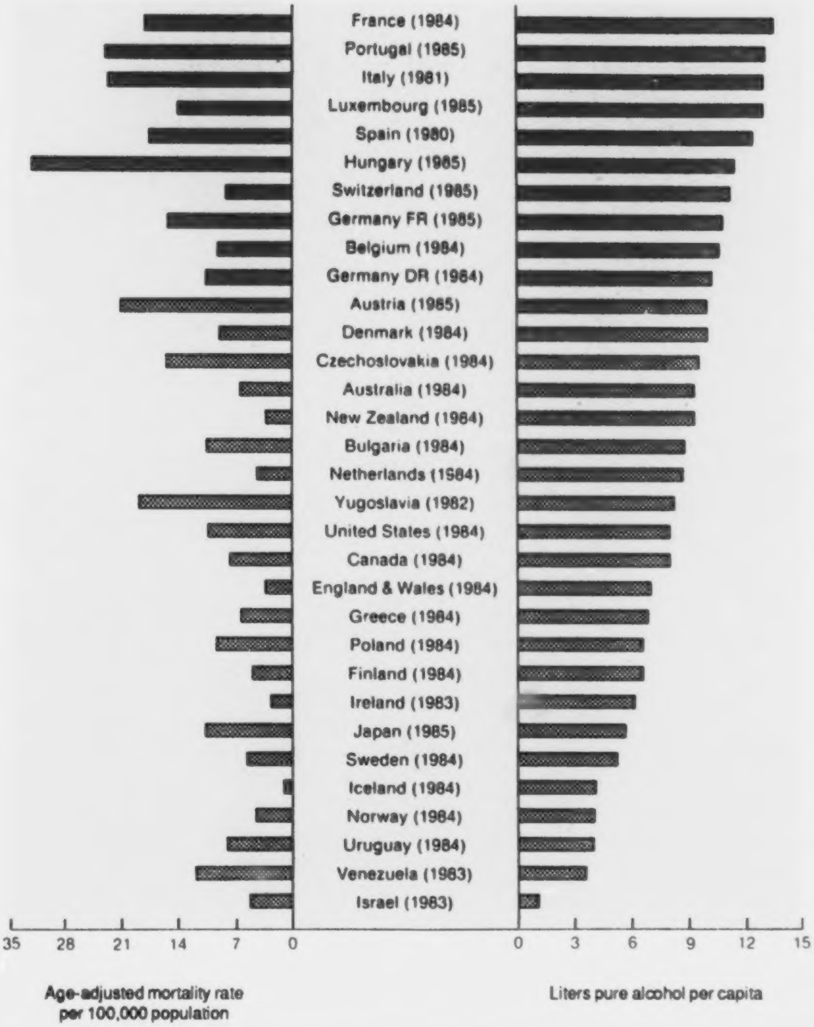

FIGURE 3. Relationship between per capita alcohol consumption and liver cirrhosis mortality rates in different countries.
SOURCE: Grant et al. 1988. Copyright 1988 by Thieme Medical Publishers, Inc.

collagen (the type most increased in dense fibrosis) was more frequent in alcohol-dependent individuals with cirrhosis than in those without cirrhosis and in controls (Weiner et al. 1988). Women seem more likely to develop alcohol-induced liver injury, which occurs with a comparatively lesser amount of alcohol ingested over a shorter period (Maddrey 1988).

Many investigators believe direct alcohol toxicity, rather than malnutrition, is responsible for these disorders. However, impaired nutrient digestion and absorption may contribute to the pathology, and alcohol itself may induce selective nutrient depletion that can cause organ damage (Maddrey 1988; Achord 1987; Lieber 1988b, 1980). Growing experimental evidence suggests that alcohol also inhibits the liver's normal repair mechanisms (Espina et al. 1988) by disrupting protein metabolism (Tuma and Sorrell 1988; Donahue et al. 1987).

New knowledge about how alcohol is metabolized in the liver may eventually improve prevention and treatment of alcohol-induced liver injury. Characteristic of alcohol-induced liver injury are lesions in the hepatic acinus, which contains functionally important liver cells (see fig. 4). The lesions typically occur in the perivenular zone (the area surrounding tiny branches or

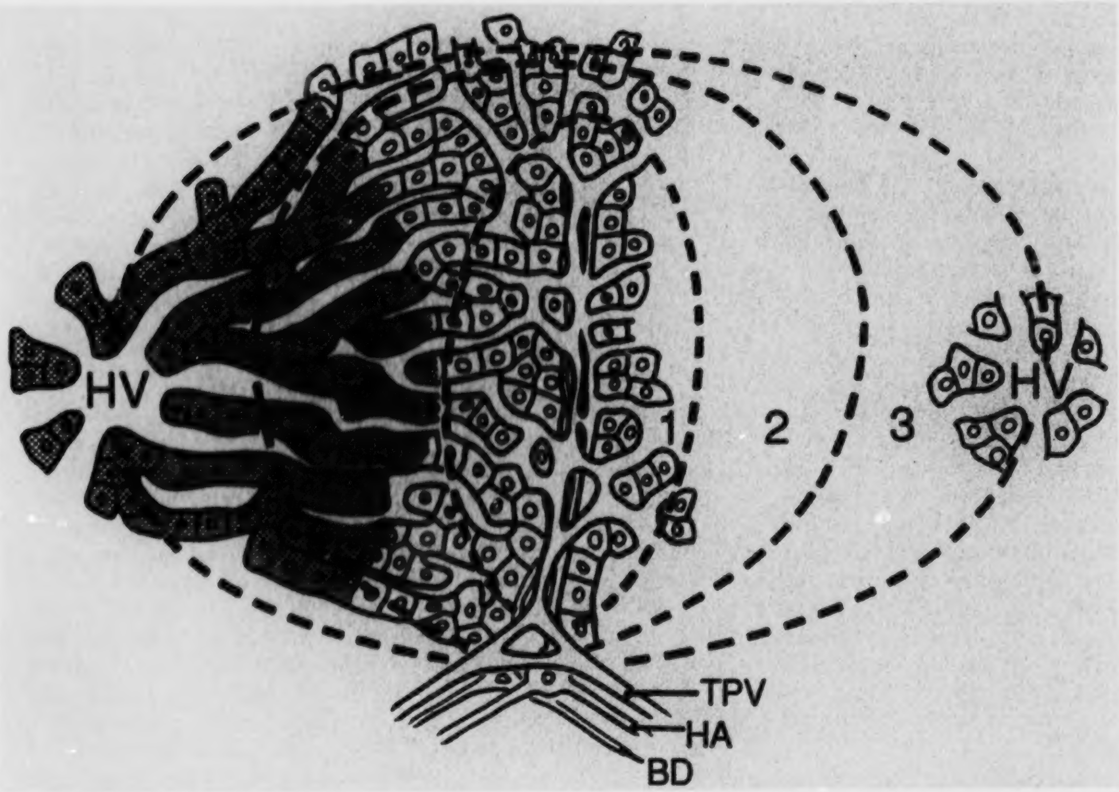

FIGURE 4. Hepatic acinus. In this structure, the liver cells process blood-borne substances delivered by way of HA (minute branches of the hepatic artery) and TPV (tiny terminal branches of the portal vein). After the blood mixes in the canals (acinar sinusoids) that interlace the cells in zone 1, it will flow through zone 2 and then into zone 3, where it will exit by way of tiny branches of the hepatic vein (HV). Bile secreted in the liver cells will be carried to the bile duct by its branches (BD).
SOURCE: Traber et al. 1988. Copyright 1988 by the American Gastroenterological Association.

venules of the portal vein) or in the centrilobular zone (the central area of the small lobe or lobule of liver tissue). These sites are farthest from the entrance point of oxygenated blood to the liver. Low oxygen tensions, which are normal in these zones, may exacerbate alcohol-induced changes in the oxidation-reduction balance in liver function (Lieber 1988c, 1984a; Israel and Orrego 1987, 1984; Jauhonen et al. 1982). Fatty acid oxidation is also decreased in these areas, which may help to explain perivenular fat accumulation. Decreased oxygen supply to the liver may have a role in the progression of alcoholic liver disease (Lieber 1988c), but one group of investigators postulates that there is decreased oxygen capacity even in the presence of ample oxygen supply (Lieber et al. 1989).

According to one theory (Israel and Orrego 1987), which proposes that lack of oxygen is the cause of liver cell injury, the alcohol-induced increase in oxygen consumption is combined with such precipitating factors as reduced hemoglobin level or interference with portal blood flow. Recent experimental findings (Lieber et al. 1989), however, point to defective oxygen utilization in the mitochondria (the cells' energy producers) rather than to lack of oxygen supply as an alcohol-induced effect.

Levels of the major alcohol-metabolizing enzyme alcohol dehydrogenase (ADH) appear to be higher in the vicinity of the perivenular zone (Buehler et al. 1982), which could increase hepatotoxicity by increasing the toxic metabolite acetaldehyde (ACH) (Lieber 1988c). ACH binds to various cellular proteins and membrane constituents (Jennett et al. 1989; Behrens et al. 1988; Mauch et al. 1986, 1987; Lieber 1984a).

Perivenular fibrosis (PVF), which can occur at the fatty liver stage in the absence of hepatitis, results from collagen deposition around venules in the liver. When the fibrotic process begins, according to some researchers, it may be a precursor to cirrhosis in humans (Lieber 1988c; Maddrey 1988); but some studies have been unable to confirm its prognostic significance (Burt and MacSween 1986; Nasrallah et al. 1980). Patients with PVF at the fatty liver stage are more likely than patients without PVF to progress to more severe stages of alcoholic liver disease if they continue to drink (Lieber 1988c).

The presence of concomitant alcoholic hepatitis, which is marked by liver tissue inflammation and liver cell death, is an important determinant of prognosis in alcoholic cirrhosis. Orrego et al. (1987) found that evidence of hepatitis in patients with cirrhosis was associated with a 270-percent increase in 1-year mortality and with a 50-percent increase in 5-year mortality. The investigators speculated that coexisting hepatitis makes the cirrhotic liver more susceptible to further alcohol damage.

At present, liver biopsy is the only reliable method of detecting PVF. Noninvasive tests are being developed based on blood measurements of substances involved in collagen metabolism; recently a radioimmunoassay to detect a modified form of type 3 procollagen was able to detect 55 to 62 percent of patients with fibrosis and more than 90 percent with cirrhosis (Lieber 1988c).

There is evidence that in alcoholic liver disease the fat-containing lipocytes in the sinusoids (terminal channels where arterial and venous blood collect) are transformed to transitional cells, which then produce collagen (Mak and Lieber 1988; Minato et al. 1983; Horn et al. 1986; Mak et al. 1984). Patients with alcohol-induced liver injury also have an increase in myofibroblasts (cells from which connective tissue develops), which synthesize collagen (Nakano et al. 1982). Furthermore, ACH and lactate, both of which increase in the liver during alcohol metabolism, increase collagen synthesis by liver myofibroblasts and human fibroblasts (Savolainen et al. 1984; Holt et al. 1984).

Mallory bodies, which are abnormal inclusions of glassy-appearing membrane structures, are found in liver cells of many patients who have severe alcoholic liver disease. Immune reactions directed against these abnormal structures may have a role in the pathogenesis of alcohol-induced liver injury (Zetterman et al. 1976), possibly causing the injury to progress (Leevy et al. 1979).

Alcohol also is metabolized in the liver, through a distinct system in liver microsomes—the microsomal ethanol oxidizing system, which is dependent on a unique alcohol-induced form of the enzyme cytochrome P450 called P450IIE1 (Lieber 1988a) (see fig. 5). P450IIE1 can activate other chemicals and may explain the increased susceptibility of heavy drinkers to hepatotoxicity from drugs and other substances (Lieber 1988c). The DNA and protein sequences for this unique cytochrome have been determined, and alcohol oxidation by purified human P450IIE1 has been demonstrated (Lieber 1988c). Ethanol oxidation by this system may have significant consequences for the pathogenesis of liver injury, either directly (through the production of ACH) or indirectly (through the microsomal activation of other chemicals) (Lieber 1988c, 1984b).

Induction of microsomal oxidizing activity enhances the production of ACH, which in turn exerts a variety of toxic effects at several sites of the hepatocytes (Lieber 1988c; Israel and Orrego 1988). ACH may link with associated proteins, forming adducts (complex compounds) that may stimulate the formation of antibodies (Lieber 1988c; Israel and Orrego 1988). Antibodies against ACH adducts are present in the serum of most alcohol-dependent individuals and may be one of the immune mechanisms responsible for alcoholic liver injury (Lieber 1988c; Israel and Orrego 1988). The highest titers of these antibodies have been found in persons with alcoholic hepatitis (Israel et al. 1988; Niemelä et al. 1987). Hoerner et al. (1988, 1986) found these antibodies against ACH adducts in more than 70 percent of alcoholic patients; the highest titers were seen in the more advanced stages of liver damage. ACH-protein adducts may also damage the function of key proteins by reacting with amino acid residues; in chronic heavy drinkers, long-term functional damage to important proteins in the liver ultimately leads to irreversible liver injury (Jennett et al. 1989).

Electron microscopy studies have revealed striking morphologic abnormalities in liver mitochondria (subcellular organelles, which are the site of energy metabolism in the cell). These abnormalities are associated with functional impairments, including decreased oxidation of fatty acids and ACH (Laposata and Lange 1986). Exposure to the resulting high ACH levels may in turn affect mitochondrial function. Functional changes in mitochondria also may produce alterations in cellular membranes. In vitro studies indicate that chronic alcohol administration alters membrane lipid composition and causes changes in the fluidity of membranes (Goldstein and Chin 1981; Rubin and Rottenberg 1982; Yamada and Lieber 1984; Polokoff et al. 1985; Kim et al. 1988). As discussed in chapter IV,

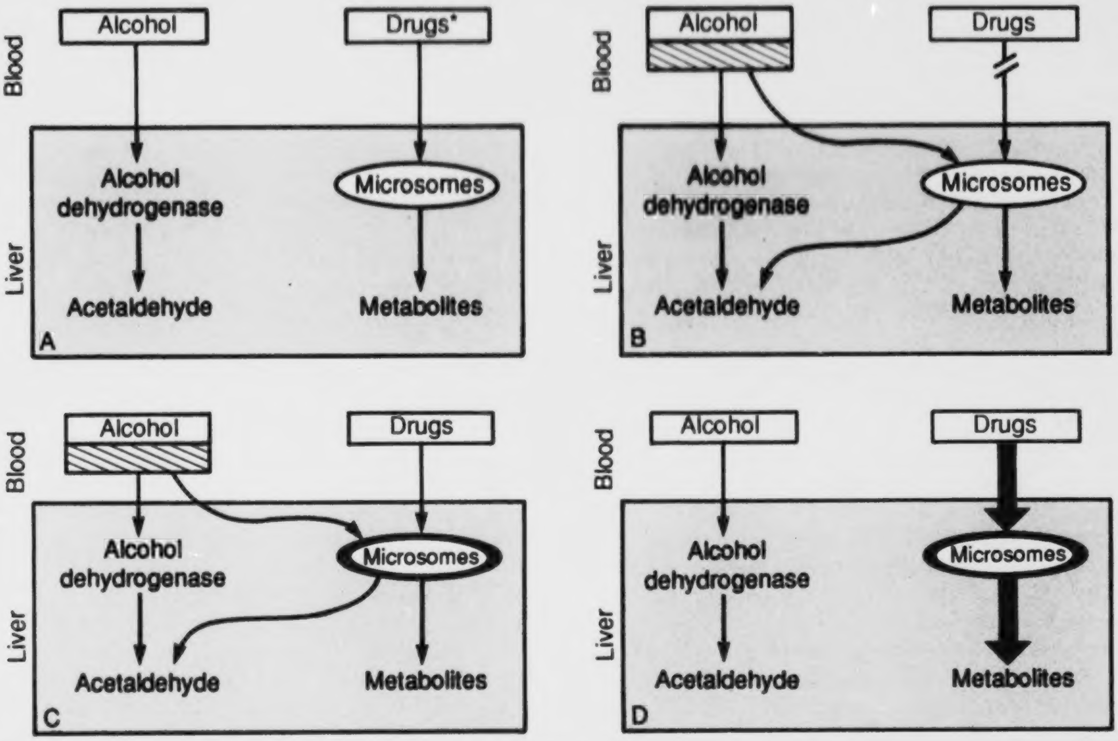
Blood
Liver
Alcohol
Drugs*
Alcohol dehydrogenase
Microsomes
Acetaldehyde
Metabolites
A
Alcohol
Drugs
Alcohol dehydrogenase
Microsomes
Acetaldehyde
Metabolites
B
Alcohol
Drugs
Alcohol dehydrogenase
Microsomes
Acetaldehyde
Metabolites
C
Alcohol
Drugs
Alcohol dehydrogenase
Microsomes
Acetaldehyde
Metabolites
D

FIGURE 5. Hepatic alcohol-drug interactions involving the ADH pathway and liver microsomes.

(A) Alcohol is metabolized by ADH, and drugs by microsomes. Hatching indicates high blood alcohol levels.

(B) Microsomal drug metabolism is inhibited in the presence of high concentration of alcohol, in part through competition for a common microsomal detoxification process.

(C) Microsomal induction after long-term alcohol consumption contributes to accelerated alcohol metabolism at high blood alcohol levels.

(D) Increased drug metabolism and activation of xenobiotics (because of microsomal induction) persist after cessation of long-term alcohol consumption.

*In this figure, "drugs" means "pharmacologic agents."

SOURCE: Lieber 1988a.

ethanol may selectively interact with particular receptive regions of cell membranes and processes that take place at the membrane surface may be particularly sensitive to the action of ethanol (Tabakoff et al. 1988).

Other early and conspicuous features of hepatic damage produced by alcohol are fat deposition and liver enlargement. Enlargement of the liver usually has been attributed to lipid accumulation, but recent research indicates that impaired protein secretion also plays a role in this process (Lieber 1988c). The enlargement of cells may have a role in compressing the hepatic sinusoids, thereby increasing resistance to the flow of venous blood through the liver and leading to portal hypertension (Orrego et al. 1981; Blendis et al. 1982; Vidins et al. 1985); this role has been disputed, however (Krogsgaard et al. 1987).

An unresolved question in patients with alcohol-induced liver disease is whether concomitant infection with hepatitis B or another virus promotes progression of liver disease (Maddrey 1988). Markers for hepatitis B have been found in some patients with alcohol-induced liver disease, especially in those with portal hypertension. In some patient populations, persons with alcoholic liver injury are more likely to have had previous viral hepatitis infection, which therefore may be a risk factor for development or progression of alcoholic liver disease (Lieber 1984a). A study by Nomura et al. (1988) suggests that an interaction between habitual alcohol intake and hepatitis B virus infection is capable of producing liver disease and that alcohol consumption intensifies the development of liver disease caused by hepatitis B virus. However, the role of concurrent infection with hepatitis B as a risk factor in alcoholic liver disease is not clear, and the literature in this area is conflicting. Some researchers have suggested that coinfection could be a risk factor for the progression of alcoholic liver disease (Hislop et al. 1981; Stigendal et al. 1984; Villa et al. 1982), but others have asserted that the presence of hepatitis B markers has no effect on the severity or progression of alcoholic liver disease (Gluud et al. 1982; Chevillotte et al. 1983; Mills et al. 1981).

Although data suggest that protein supplements tend to speed recovery of nutritional status and improvement in liver function tests in alcoholic liver disease, there have been no major confirmed differences noted between treatment and control groups after 3 to 4 weeks (Achord 1987). Caloric infusions may be indicated in alcohol-dependent individuals who have a reversible component to their liver disease but who cannot consume adequate diets (Achord 1988). Propylthiouracil, an antithyroid drug, reduces the hypermetabolic state induced by alcohol administration and has been shown experimentally to protect against alcohol-induced hepatocellular necrosis in hypoxic (low-oxygen) conditions (Orrego et al. 1987). In a study of patients with alcoholic liver disease treated with propylthiouracil for 2 years, Orrego et al. (1987) found a significant reduction in mortality—approximately two-thirds less than in a placebo group. However, there was an apparent lack of protection in heavy drinkers. A postulated mechanism of action for propylthiouracil's therapeutic effectiveness is that it decreases or abolishes the alcohol-induced increase in oxygen consumption by the liver and increases the delivery of oxygen to the liver by increasing portal blood flow (Orrego and Carmichael 1989).

Liver transplantation is a therapeutic modality that has been used successfully for advanced or end stage alcoholic liver disease. In a major ongoing study of liver transplantation, the 1-year survival rate of 73 percent and 2-year survival of 64 percent in patients with alcoholic liver disease did not differ from survival rates for nonalcoholic controls (Starzl et al. 1988; Kumar et al. in press). Further, recidivism to alcoholism has been quite low (Starzl et al. 1988; Van Thiel et al. 1989).

Thurman et al. (1988) reported that pharmacologic agents that block cellular uptake of calcium, such as those used to treat cardiovascular disease, protect the liver from damage by a variety of chemicals (including alcohol). They also found that one type of calcium entry blocker (nitrendipine) protects against hypoxic damage induced by ethanol in the perfused rat liver. These studies have possible clinical importance, although extensive studies evaluating protection against alcoholic liver injury by calcium entry blockers have not yet been done.

Effects on the Gastrointestinal Tract

Regular alcohol consumption may precipitate inflammation of the esophagus and exacerbate existing peptic ulcers (Miller and Gold 1987; Kurata and Halle 1984). The relative risk of esophageal cancer is higher in alcohol abusers, as is the incidence of chronic atrophic gastritis, a precursor of gastric carcinoma. Smoking, often seen in these patients, may contribute to the cancer development.

Until recently it had been thought that very little alcohol is metabolized in the stomach (Lamboeuf et al. 1981, 1983; Lin and Lester 1980). However, it has been found that a significant fraction of alcohol in doses comparable to "social drinking" amounts (0.15 grams per kilogram, or approximately the amount of alcohol in a typical drink) is metabolized in the stomach before entering the systemic circulation (Julkunen, Di Padova, and Lieber 1985; Julkunen, Tannenbaum, et al. 1985; Di Padova et al. 1987). In rats, about 20 percent of ethanol administered in a low dose is metabolized in the stomach (Caballeria et al. 1987). In alcohol-dependent individuals, initial metabolism of alcohol in the stomach is virtually nonexistent when alcohol is ingested after fasting, so that much more alcohol enters the systemic circulation (Di Padova et al. 1987). This reduced metabolism in alcohol-dependent individuals may be due to diminished gastric ADH activity (Julkunen, Di Padova, and Lieber 1985; Julkunen, Tannenbaum, et al. 1985).

Under normal conditions in nonalcohol-dependent individuals, gastric ADH and associated alcohol metabolism decrease the bioavailability of alcohol. Thus a "barrier" to the penetration of alcohol into the body is formed, which could modulate the potential toxicity of alcohol. After chronic alcohol consumption, much of that barrier appears to be lost, so that systemic effects of alcohol are exacerbated. The barrier is also affected by some pharmacologic agents (such as the antiulcer agent cimetidine), which decrease the activity of gastric ADH (Caballeria et al. 1989).

The stomach is a site where alcohol causes significant damage in humans because it is exposed to higher concentrations of alcohol than any other site, with the possible exception of the mouth and the esophagus. Alcohol slows gastric emptying, interferes with the action of gastroesophageal sphincters, stimulates gastric secretion, and often injures the gastric mucosa (inner lining), especially when combined with aspirin. Damage to the stomach lining appears to be partly due to alcohol's ability to disrupt the protective mucus that coats the gastric mucosa, perhaps by interfering with its synthesis. Mucosal injury of the stomach may also occur through damage to junctions between the mucosal cells, leading to back diffusion of acid that damages blood vessels or the mucosa and submucosa (Szabo et al. 1985).

The delay in gastric emptying caused by alcohol may involve depression of gastric smooth-muscle activity, and it is possible that similar effects of alcohol may occur in smooth muscle throughout the gastrointestinal tract.

Alcohol also produces alterations in intestinal motility and mucosal function that result in malabsorption. It affects peristalsis acutely through neurohumoral disturbances and chronically through neuropathic changes (Mayer et al. 1978; Winship et al. 1968). A variety of structural and functional changes in the intestinal mucosa have been described following alcohol injury, including flattening of intestinal villi (microscopic projections from intestinal mucosal cells that increase the absorptive surface), loss of certain enzymes (disaccharidases), and inhibition of amino acid and glucose transport mechanisms (Dinda et al. 1977). Alcohol's effect on intestinal mucosal cells increases their permeability to large molecules that would otherwise not be absorbed, indicating cell damage. Ishii et al. (1988) reported that chronic alcohol feeding in rats results in a significant increase in intestinal activity of the enzyme gamma-glutamyl transpeptidase (GGTP). This study suggests that the increased serum GGTP activity frequently seen in alcohol-dependent persons may originate in part from enhanced activity of the enzyme in the intestine.

Heavy alcohol consumption and gallstones are the two leading causes of acute pancreatitis (Fuller 1988). Acute pancreatitis is manifested by severe abdominal pain (usually upper abdominal) often accompanied by nausea, vomiting, fever, and tachycardia. The blood tests, serum amylase and lipase, are useful in helping to make the diagnosis, as are the relatively new imaging tests, ultrasonography and computerized tomography, which represent major advances for establishing this diagnosis (Fuller 1988). Most patients having acute pancreatitis respond within a few days to standard treatment involving intravenous fluids and analgesics (McPhee 1985). Approximately 20 percent of patients, however, experience a severe form having one or more complications and a protracted course, and some episodes of acute pancreatitis are fatal; the mortality rate for alcoholic acute pancreatitis is under 5 percent. Although the causal mechanism is unknown, animal studies suggest that activation of potent pancreatic enzymes within the pancreas itself (rather than in the lumen of the small bowel where such activation normally occurs) may be involved (Steer et al. 1984). Other studies have implicated acetaldehyde, the metabolite of ethanol, as having a toxic effect on the pancreas (Geokas et al. 1985).

Heavy alcohol consumption is a principal cause of chronic pancreatitis. More than 75 percent of patients with chronic pancreatitis have a history of heavy alcohol consumption (Van Thiel et al. 1981; Lipsitz et al. 1981), and the disease typically appears after 5 to 10 years of heavy alcohol use (Sarles 1971). The abdominal pain caused by this disease is severe and, if chronic, can sometimes be relieved by surgical removal of the pancreas. Little is known about the pathogenesis of chronic pancreatitis in alcohol-dependent individuals, partly because the location of the pancreas makes study of its function difficult and partly because the disease typically remains hidden for a long time. By the time alcohol-dependent individuals with this disorder present with abdominal pain, chronic changes have already occurred in the pancreas. Attacks of pain can recur even if drinking has ceased.

Within 3 or 4 years of the initial attack, many of these patients develop pancreatic hormone deficiencies. As chronic exposure to alcohol reduces the flow of pancreatic digestive enzymes into the small intestine, absorption of nutrients is reduced and the patient suffers from malnutrition. At the same time, regulation of sugar metabolism is disrupted because the pancreas fails to secrete enough insulin and glucagon into the patient's bloodstream, thus increasing the risk of diabetes.

Although one retrospective study of alcoholic-dependent individuals with pancreatitis showed that they had been drinking about 160 grams of alcohol a day (approximately 12 standard drinks), data are lacking on what minimum level of drinking causes the disease to develop. There appears to be large individual variability in susceptibility to the development of pancreatitis. Mezey et al. (1988) found that women with chronic pancreatitis had consumed alcohol for a shorter period than men, although there was no sex difference in the total daily amount of alcohol consumed.

The role of nutritional factors in chronic pancreatitis is uncertain. Studies in France have indicated that alcoholic pancreatitis is more likely in persons who consume a high-protein diet, but Mezey et al. (1988), who studied pancreatitis in subjects who consumed more than 50 percent of their calories as alcohol, concluded that high dietary intake of protein and fat is not a factor in the development of chronic pancreatitis in alcohol-dependent individuals.

A problem that seriously hinders the study of alcoholic chronic pancreatitis is the lack of a suitable animal model. In one study (Singh et al. 1982), rats that were administered alcohol for 30 months exhibited pancreatic changes, but other investigators have found only accumulations of lipid droplets and some ultrastructural changes in pancreatic cells of rats fed alcohol up to 54 months; nothing resembling human chronic pancreatitis was seen.

Most theories about the pathogenesis of alcoholic pancreatitis incorporate the effects of alcohol on pancreatic secretion. These effects vary, depending on whether alcohol intake is chronic. Thus alcohol administration decreases pancreatic secretions in alcohol-naive animals and humans, but it increases those secretions in animals and humans that have been chronically exposed to alcohol. There is evidence that alcohol's stimulation of pancreatic secretions combined with obstruction of flow of these secretions from the pancreas may lead to pancreatic cell death (necrosis) and eventually to atrophy and replacement of pancreatic cells with scar tissue (fibrosis).

One possible explanation for pancreatic cell destruction is that the pancreas is attacked by the very enzymes it produces. There is evidence that alcohol reduces the levels of natural inhibitors that normally prevent zymogens, the precursors of digestive enzymes, from being converted into active enzymes in the pancreas. Trypsin is one of these enzymes, and alcohol has been shown to cause a decrease in the factors that inhibit trypsin activity in the pancreas. In addition, chronic pancreatitis patients have increased levels of the types of digestive enzymes that are released by lysosomes, microscopic bodies that normally defend their host cells against bacteria and other cell-threatening agents (Steer et al. 1984).

Recent work has suggested that the production of oxygen free radicals, a highly reactive form of oxygen, may be one of the early stages in the pathogenesis of pancreatitis. Research results also indicate that the free radical scavengers, as well as the anti-gout pharmaceutical allopurinol (an inhibitor of the oxidase enzyme that presumably produces the free radicals), attenuate the extent of the disease in experimental animals.

In summary, pancreatitis may develop through the combined effects of stimulation of pancreatic secretion and obstruction of secretory flow into the duodenum. Permanent obstructive alterations in the pancreatic duct may develop in turn. In addition, direct injury to the pancreas may result from premature activation of enzyme precursors (zymogens), so that their digestive action occurs in that organ, producing inflammation, necrosis, and fibrosis.

Nutritional and Metabolic Disorders

Alcohol may account for more than 10 percent of the total caloric intake of adult drinkers in the United States (Williamson et al. 1987). In examining the association between alcohol and body weight, Williamson et al. (1987) found that alcohol has a substantial association with lower body weight in women, similar to the effect of smoking. Compared with nondrinkers, women who consumed alcohol 7 to 13 times a week weighed about 3.6 kilograms (about 8 pounds) less. However, alcohol use diminished the weight-lowering effect of smoking in men. The mechanisms underlying these findings are unclear.

Malnutrition resulting from poor eating habits, a frequent complication of alcohol dependence, can arise from reduced overall food intake as well as from deficiencies of specific nutrients. Results of nutritional deficiencies include anemia, neuropathy, Wernicke's disease, and depressed cellular and hormonal functions. Nutritional deficiencies also may contribute to the fetal alcohol syndrome, liver disease, pancreatic disease, malabsorption, and carcinogenesis. Fasting and a zinc-deficient diet decrease the activity of the important alcohol-metabolizing enzyme ADH, a zinc-containing enzyme.

Alcohol interferes with the metabolism of most vitamins; the deficiencies of thiamine, folate, pyroxidine, vitamin A, and zinc that are common in alcohol-dependent individuals may result from impaired absorption as well as from poor nutrition. There is considerable evidence that alcohol can impair active transport mechanisms for nutrient absorption. Alcohol is known to interfere with the absorption of many nutrients, including amino acids, glucose, choline, zinc, and vitamins (Mezey 1985a). The physiologic significance of the malabsorptive effects is uncertain, however, because there is an excess of intestinal absorptive capacity, as seen in individuals who have had large segments of the intestine surgically removed but still maintain adequate nutrition.

Nevertheless, abnormal metabolism of proteins, carbohydrates, lipids, vitamins, and minerals occurs with heavy, chronic alcohol consumption (Sherlock 1984; Mezey 1985a). Alcohol ingestion interferes with the metabolism of most vitamins, including folic acid. Ingestion of alcohol produces a fall in serum levels of folic acid, possibly by increasing its hepatic uptake and storage in a polyglutamate form and decreasing its intrahepatic circulation (Hillman et al. 1977). ACH has been shown to interfere with pyridoxine metabolism by displacing the vitamin from its binding sites and accelerating its subsequent metabolism (Lumeng and Li 1974).

Alcohol also has profound metabolic effects on carbohydrate, lipid, and protein metabolism. Ethanol is known to inhibit gluconeogenesis (synthesis of glucose from noncarbohydrates), but the mechanism of ethanol-induced hyperglycemia is obscure (Mezey 1985b; Lieber 1984b). Although the pathophysiology of alcoholic ketoacidosis (excess blood acidity caused by organic acids) has been well described, the reasons why individuals vary in susceptibility to this condition are not understood (Lieber 1982; Williams 1984; Halperin et al. 1983).

Little work has been done on the relation of heavy alcohol consumption to the development of metabolic bone disease, although it is known that alcohol stimulates both urinary calcium and magnesium excretion. Osteoporosis in young and middle-aged men has been associated with chronic alcohol use. Peng et al. (1988) demonstrated in rats that a relationship exists between bone strength and alcohol consumption; alcohol consumption resulted in weaker femurs compared to controls. The investigators postulated that the mechanism responsible for decreased bone strength in alcohol-fed rats may underlie the increased incidence of fractures in human alcohol-dependent individuals.

Alcohol-dependent persons are also susceptible to acute and chronic muscle injury. Biopsy-proved muscle fiber atrophy has been found in 60 percent of such individuals (Peters et al. 1985; Martin et al. 1985). The quantity of alcohol consumed in the year before biopsy correlated significantly with the severity of the atrophy (Peters et al. 1985). The atrophy was not associated with vitamin deficiencies and was independent of any existing neuropathy, although it was more likely to be seen in patients with severe liver disease, peripheral neuropathy, or malnutrition. Sequential studies in abstaining alcohol-dependent individuals showed significant improvement in muscle within 3 months and often complete recovery within a year (Peters et al. 1985). The etiologies of these syndromes are incompletely understood, although it is believed that alcohol may be directly toxic to muscle (Haller and Knochel 1984; Martin et al. 1985).

Effects on the Cardiovascular System

Chronic alcohol abusers may develop clinical signs of cardiac dysfunction, and up to 50 percent of the difference between normal death rates and those of alcohol-dependent individuals and heavy drinkers may be attributed to cardiovascular disorders (Altura 1986). Alcohol abuse affects the cardiovascular system in several ways. Alcohol can affect the heart muscle itself, producing cardiomyopathy (degeneration of the heart muscle) and cardiac arrhythmias. Chronic alcohol consumption is associated with a significant increase in hypertension and may play an important role in ischemic heart disease (deficient blood circulation to the heart) and cerebrovascular disorders, including stroke. Some survey data suggest that moderate alcohol intake may have an ameliorating influence on the development and progression of atherosclerosis by changing the lipid composition of the blood, but this issue requires further research.

The Heart

Acute alcohol administration causes numerous biochemical changes in the heart muscle (myocardium), including a reduction in fatty acid oxidation (the primary fuel source for the heart) and an increase in triglyceride content (Kako et al. 1973).

Recent studies show that the heart directly metabolizes ethanol to form a class of compounds called fatty acid ethyl esters and that these compounds may induce dysfunction in the mitochondria (energy-producing structures of the heart) (Lange and Kinnunen 1987; Klatsky 1987). This metabolic pathway may be a direct link between alcohol ingestion and the development of alcohol-induced cardiomyopathy.

Impaired uptake and binding of calcium by the sarcoplasmic reticulum (a subcellular membrane structure) has been observed in animal models of alcohol dependence, and the flux of calcium ions necessary for contractility is also impaired (Regan and Morvai 1987). Electron microscopy studies of cardiac muscle damaged by alcohol show characteristic changes, including a depletion in contractile proteins and increased numbers of disrupted mitochondria (Benzer 1987).

Many studies have demonstrated that alcohol can depress myocardial contractility, especially in persons with preexisting cardiac disease (Lange and Kinnunen 1987; Klatsky 1987). People with a long history of alcohol abuse but no clinical evidence of heart disease, especially men, often are shown by physiologic studies and noninvasive testing to have abnormal cardiac function, which may indicate preclinical alcoholic cardiomyopathy (Klatsky 1987). Furthermore, up to half of all people with idiopathic (unexplained or spontaneous) cardiomyopathy in the United States are alcohol dependent (Wang et al. 1987). These findings suggest that a substantial number of alcohol-dependent individuals may have some degree of cardiac impairment.

In a recent report, Urbano-Marquez et al. (1989) concluded that the extent to which alcohol is toxic to skeletal and cardiac muscle depends on the amount of alcohol consumed. In their study of 50 asymptomatic alcoholic men (mean age 38.5 years), skeletal and cardiac muscle strength and cardiac function declined as the estimated total lifetime dose of ethanol increased.

Clinical manifestations of idiopathic and alcohol-induced cardiomyopathy do not differ, but prognosis does, making differentiation of these disorders essential (Wang et al. 1987). The prognosis of idiopathic cardiomyopathy is poor regardless of treatment, but alcoholic cardiomyopathy may have a good prognosis if marked reduction in alcohol use occurs (Wang et al. 1987). Alcohol-induced cardiomyopathy may be reversible in about 30 percent of patients if they become abstinent. Recovery without abstinence is rare (Lange and Kinnunen 1987).

Alcohol-induced myocardial toxicity can be potentiated by cofactors. Two documented epidemics of acute cardiac failure in heavy beer drinkers occurred following consumption of beer that contained arsenic and cobalt; the amounts of these substances themselves were insufficient to account for the heart damage (Klatsky 1987).

A number of studies indicate that irritability of the heart muscle in alcohol-dependent individuals is increased, during both drinking and acute withdrawal, and that arrhythmias can result. In the ventricles, the blood-pumping chambers of the heart, abnormally rapid contractions and irregular quivering are more common with elevated blood alcohol concentrations in the presence of underlying organic disease. A study by Koskinen et al. (1987) suggests that alcohol plays a significant role in the genesis of otherwise unexplained rapid, uncoordinated movements of the heart atria, which receive blood. Among 35 young and middle-aged patients with new-onset idiopathic atrial fibrillation, significantly more had consumed alcohol within 2 days of the onset of the arrhythmia compared to patients with nonidiopathic atrial fibrillation and to a control group. The investigators suggested that in 15 to 30 percent of patients with idiopathic atrial fibrillation the arrhythmia may be alcohol related and that between 5 and 10 percent of all new episodes of atrial fibrillation can be explained by alcohol use (Koskinen et al. 1987).

The "holiday heart syndrome," episodes of abnormal cardiac rhythms following several days of heavy drinking (including both atrial and ventricular dysrhythmias), has been seen in chronic alcohol drinkers, with and without underlying cardiomyopathy (Ettinger et al. 1978). Because this syndrome appears after the binge rather than during the period of intoxication, it may be associated with a mild alcohol withdrawal syndrome or be mediated via the central nervous system (CNS) (Lange and Kinnunen 1987). Acute ethanol infusion can prolong conduction times in both the atrium and the ventricle in patients prone to alcohol-induced dysrhythmias (Engel and Luck 1983), but little is known about the exact mechanism whereby alcohol disrupts the heart's electrical conduction system.

There is also evidence suggesting that moderate levels of alcohol consumption can precipitate coronary artery spasms in patients with variant angina, a type of angina pectoris in which painful spasms occur during rest (Ettinger et al. 1978). In animal experiments, small amounts of alcohol cause contractions in isolated coronary arteries. It therefore appears likely that alcohol is capable of precipitating angina in individuals who are otherwise susceptible to it.

The Vascular System

In addition to possible direct action on the heart, alcohol may alter circulatory function by affecting the release and actions of hormones and humoral substances, such as catecholamines, aldosterone, cortisol, dopamine, angiotensin 2, renin, eicosanoids, and cyclic adenosine monophosphate, among others (Altura 1986). Changes in the activity or secretion of these substances may alter cardiac activity, blood pressure, blood flow, and vascular homeostasis and may eventually result in cardiac and vascular damage.

Numerous epidemiologic studies around the world have found that alcohol abuse is associated with hypertension (Lange and Kinnunen 1987; Klatsky 1987). Estimates of the proportion of hypertension associated with alcohol vary from 5 to 24 percent (Klatsky 1987). Moderate alcohol consumption appears to produce moderate increases in blood pressure, and alcohol-dependent individuals may have considerably higher than normal blood pressure. Many cases diagnosed as idiopathic or essential hypertension (high blood pressure having no known cause) may actually have chronic alcohol ingestion as their cause (Miller and Gold 1987; Benzer 1987).

The alcohol-hypertension relationship is seen mostly at drinking levels equivalent to a usual daily intake of three or more drinks and is strongest in men, Caucasians, and people over age 55 (Klatsky 1987). In a large epidemiologic study the prevalence of hypertension, defined as blood pressure of 160/95 mm Hg or more, doubled in white individuals who drank six or more drinks a day compared to nondrinkers or persons who had two or fewer drinks daily (Klatsky 1987).

Blood pressure often increases substantially during and shortly after acute intoxication (Lange and Kinnunen 1987). When a single episode of consumption or dose of alcohol is followed by withdrawal, blood pressure is normally increased by activity in the sympathetic nervous system (the "fight or flight" system that has stimulating effects like those of a shot of adrenaline) (Miller and Gold 1987). Increases in norepinephrine metabolites are found even after modest alcohol ingestion (Lange and Kinnunen 1987).

Alcohol withdrawal has been proposed as a factor in the increases in blood pressure, and several studies have found increased metabolic correlates of blood pressure during withdrawal, such as norepinephrine, arginine vasopressin, and renin (Criqui 1986). However, indirect effects such as psychosocial stress, environmental factors such as diet, and genetic predisposition to alcohol-induced hypertension cannot be ruled out (Klatsky 1987). Data suggest that substantial or complete regression in hypertension may occur in some individuals when they abstain (Klatsky 1987; Criqui 1986; Miller and Gold 1987; Benzer 1987).

Ongoing clinical studies throughout the world indicate a higher than normal incidence of hemorrhagic stroke and other intracranial bleeding among heavy users of alcohol (Altura 1986). Such stroke-like episodes often appear within 24 hours of a drinking binge, and several investigators have suggested that excessive alcohol consumption predisposes to stroke and sudden death (Altura 1986). In a recent prospective study among middle-aged women, Stampfer et al. (1988) found that moderate alcohol consumption, defined as three to nine drinks a week, was associated with increased risk of a hemorrhage beneath the arachnoid membrane, which is the middle one of three membranes covering the brain and the spinal cord. In animals, moderate amounts of alcohol can cause spasm in cerebral blood vessels (Altura et al. 1983). The alcohol-stroke relation may be partially explained by association of both drinking and stroke with hypertension and by a bleeding tendency due to alcohol (Klatsky 1987).

Coronary Heart Disease

The question whether moderate drinking protects against coronary heart disease, a pathological condition in the arteries that supply blood to the heart muscle, continues to generate controversy. Several epidemiologic studies have reported that moderate drinking (up to one or two drinks a day) may reduce the risk of coronary heart disease below that found in abstainers (Lange and Kinnunen 1987; Klatsky 1987; Moore and Pearson 1986). In a recent large-scale prospective study of middle-aged nurses, Stampfer et al. (1988) found that moderate alcohol consumption (three to nine drinks per week) was associated with decreased risk of coronary heart disease and ischemic stroke. On the basis of a large-scale prospective study of middle-aged British men, Shaper et al. (1987) questioned whether alcohol has any direct protective effect against ischemic heart disease. Shaper and colleagues found that although the light daily drinkers had the lowest incidence of ischemic heart disease events, they also contained the lowest proportion of current smokers, had the lowest mean blood pressure, had the lowest mean body index, and contained the lowest proportion of manual workers. Shaper et al. (1987) concluded that these characteristics are more likely to account for the apparent protective effect of alcohol.

On the other hand, numerous studies have also shown that the risk of coronary artery disease and coronary artery disease mortality is increased by heavy drinking (Altura 1986; Moore and Pearson 1986).

One mechanism proposed to account for the apparent protective effect of alcohol is that higher levels of high-density lipoprotein (HDL), which are associated in other studies with decreased risk of coronary artery disease, occur with alcohol consumption. Okamoto et al. (1988) found that serum levels of HDL were elevated in habitual alcohol drinkers without liver injury but were reduced in those with liver disease—markedly so in those with cirrhosis. Recent studies have indicated that the subfraction of HDL that is alcohol sensitive is HDL3, a nonprotective subfraction; HDL2, which is associated with decreased risk of coronary heart disease, is marginally elevated by ethanol (Lange and Kinnunen 1987; Criqui 1986; Moore and Pearson 1986). Thus any protective effect of alcohol for coronary heart disease may be independent of an HDL effect.

However, other recent evidence suggests that apolipoproteins (components of HDL) may be important indicators of atherosclerosis and coronary artery disease and that these are increased by moderate alcohol consumption (Moore and Pearson 1986). Okamoto et al. (1988) found that apolipoprotein A-1 was elevated in drinkers without liver injury but that apolipoprotein A-2 was not.

Alcohol's effects on blood-clotting factors have also been suggested as a possible protective mechanism. Low doses of alcohol might prevent the increased blood clotting, coagulation of blood platelets, and generation of thromboxane B2 associated with cardiovascular disorders (Stampfer 1988; Criqui 1986). However, recent reports have also indicated that low doses of ethanol can enhance aggregation of blood platelets and lead to generation of thromboxane B2 (Altura 1986). In another possible mechanism, moderate alcohol may directly affect coronary artery diameter and coronary blood flow (Moore and Pearson 1986).

Effects on the Immune System

It is difficult to assess the primary effects of alcohol on the immune system in human beings because concurrent malnutrition, infection, liver disease, and other disorders may independently affect this system. However, many clinical studies have reported increased susceptibility to infection in alcohol-dependent individuals and the lack of normal response to infection in experimental animals (Johnson 1975; Adams and Jordan 1984; Cotle et al. 1982; Andersen 1975; Gluckman et al. 1977).

Chronic alcohol consumption appears to depress the production of polymorphonuclear leukocytes (PMNs) in the bone marrow. Defects in the movement and aggregation of these white blood cells (normal responses to infection) have been reported in patients with alcoholic liver disease, perhaps accounting for these patients' increased susceptibility to bacterial infection (Rajkovic et al. 1984). In vitro experiments show that alcohol impairs the ability of PMNs to adhere to cell surfaces, an essential step in their migration to the site of inflammation (MacGregor et al. 1974; Brayton et al. 1970; Gluckman and MacGregor 1978). A reduced number of granulocytes (granulocytopenia) is seen in up to 8 percent of alcohol-dependent individuals admitted to hospitals, especially those with infection (Liu 1973). Granulocyte numbers return to normal after alcohol withdrawal.

Lymphocyte proliferation responses are also lower in alcohol-dependent individuals without liver disease, suggesting that some changes in immune function observed in alcohol-dependent individuals are linked to the direct effects of alcohol on the immune system rather than to the associated liver disease (Mutchnick and Lee 1988). The possibility has also been raised that autoimmunity may play a role in the pathogenesis of alcoholic liver disease (Johnson and Williams 1986).

Cell-mediated immunity is significantly inhibited by alcohol, as exemplified by the high incidence of tuberculosis among alcohol-dependent individuals (Smith and Palmer 1976). The incidence of virus-associated head and neck cancers is also high in alcohol-dependent individuals, suggesting that heavy drinking may cause some loss of cell-mediated immunity against these viruses (Martinez 1970). In alcohol-dependent persons with severe liver disease, T-lymphocytes (a type of white blood cells that fight infection) are reduced in number and are deficient in their ability to undergo blast transformation in response to substances (mitogens) that induce blast formation and synthesis of DNA and RNA (Roselle and Mendenhall 1984; Lundy et al. 1975). This inability is associated with poor response to test antigens and failure to develop immune responsiveness to new antigens. Incubating lymphocytes from nonalcohol-dependent individuals with alcohol leads to similar failure of transformation, cytotoxic T-cell activity, and migratory movement (Roselle and Mendenhall 1982; Glassman et al. 1985; Ristow et al. 1982; Kaelin et al. 1984).

Chronic alcohol administration reduces the T-cell population in lymphoid tissue and the peripheral blood and spleens in experimental animals, but the proportion of T-helper cells in the spleen is increased. Thus it is suggested that immunosuppression and transient imbalances in components of cellular immunity induced by alcohol may play a role in immune disorders associated with alcohol dependence (Mufti et al. 1988). On the basis of animal experiments, Bagasra et al. (1987) suggested that suppressor T-cells are probably the most susceptible to alcohol effects, followed by the helper T-cells. Many alcohol-dependent individuals have increased immunoglobulin levels and increased auto-antibodies, probably due to the effect of liver disease on B-cells (Ladefoged et al. 1979). Alcohol itself can inhibit the function of B-lymphocytes (which carry immunoglobulins and produce antibodies) from humans and experimental animals (Gilhus and Matre 1982; Jerrells et al. 1986; Aldo-Benson 1988). This inhibition may be a factor in the increased incidence of pneumonia and peritonitis in alcohol-dependent individuals (Smith and Palmer 1976). Grossman et al. (1988) suggested that alcohol may alter the processes of maturation and replication of lymphocytes in the spleen.

Alcohol also may have an adverse effect on natural killer cells, which can mediate cell-destructive reactions without having to be sensitized by previous exposure to their target and which seem to be important in the body's defense against spontaneously arising tumors and metastases. This function can be impaired by malnutrition and alcoholic liver disease. Abdallah et al. (1988) found a reduction of greater than 50 percent in mice that were fed alcohol chronically, although other studies have reported both increased and decreased activity (Abdallah et al. 1988).

Alcohol impairs phagocytosis (killing of bacteria by white blood cells) (Roberts and Segal 1987) and inhibits antibody-dependent cell-mediated cytotoxicity in mouse spleen cells (Walia et al. 1987). Alcohol interferes with cell lysis by reacting with sites that are required for triggering the lytic event (Walia et al. 1987).

No evidence exists to indicate a direct association between alcohol use and the development of acquired immune deficiency syndrome, although by reducing inhibitions alcohol use may lead to an increase in risk-taking behavior, such as sharing needles among drug users. However, alcohol could increase the risk of primary infection when individuals are first exposed to the human immunodeficiency virus (HIV). For individuals already infected with HIV, alcohol could result in progression from asymptomatic to clinical infection by depressing the immune mechanisms that act to limit the negative impact of HIV (MacGregor 1987). A recent epidemiologic study, however, did not reveal an alcohol-associated acceleration of HIV-related disease (Kaslow et al. 1989).

Alcohol and Cancer

There is considerable epidemiologic evidence that alcohol abuse is associated with increased risk of certain kinds of cancers, especially those of the liver, esophagus, nasopharynx, and larynx (Driver and Swann 1987; Tuyns 1979; Decker and Goldstein 1982). The incidence of such cancers is notably lower in religious groups who abstain from alcohol use (Driver and Swann 1987). Studies have suggested that risk of esophageal cancer increases with alcohol use (Tuyns 1979) and that chronic atrophic gastritis, a precursor to gastric cancers, occurs frequently in alcohol abusers. However, the literature on the relationship between cancer of the stomach and alcohol consumption is inconclusive (Driver and Swann 1987). Within certain geographic areas, consumption of beer in particular correlates with the appearances of cancers in the lower gastrointestinal tract, suggesting that nonalcohol ingredients (congeners) in alcoholic beverages may play a role in development of these tumors (National Research Council 1982; Driver and Swann 1987). A recent report on large-scale epidemiologic studies in Japan noted that daily drinking consistently elevated the risk for prostate cancer (Hirayama 1986). There is no definitive evidence linking breast or lung cancer with chronic alcohol use; the fact that these are among the most common human cancers suggests that alcohol does not play a systemic role in carcinogenesis (Webster et al. 1983; Lieber et al. 1979). Large-scale epidemiologic studies linking alcohol and breast cancer have been criticized for methodological shortcomings (Feinstein 1988). In a review of reports from 1974 to 1987 linking alcohol consumption with breast cancer, Lowenfels and Zevola (1989) noted that three prospective studies showed slightly higher risk of breast cancer for consumers versus nonconsumers of alcohol but that the results of correlation and case-control studies had been inconsistent. In both positive and negative studies, the amount of alcohol consumed by women with breast cancer was low. More research is needed to provide definitive information on the relationship between alcohol use and breast cancer.

Although liver cancer in alcohol-dependent individuals has been thought to result from cirrhosis (Tuyns 1979; Lieber et al. 1979) or an association with hepatitis B virus infection (Ohnishi et al. 1987), there is increasing evidence of possible direct effects of alcohol on liver carcinogenesis (Driver and Swann 1987). The reported proportion of alcohol-dependent individuals with cirrhosis who develop cancer ranges from 5 to 30 percent (Driver and Swann 1987).

Alcohol does not act as a complete carcinogen in that it does not directly damage genes (Driver and Swann 1987; Weisburger and Williams 1981). However, ethanol may act during tumor initiation and progression. Alcohol may affect enzymes controlling carcinogens—as evidenced by the seemingly synergistic effect of alcohol consumption and smoking in the development of cancers, especially those of the head and neck (Lieber 1988c; Driver and Swann 1987; McCoy and Wynder 1979). One study has found that the relative risk for esophageal cancer is much higher when daily drinking is combined with smoking 25 or more cigarettes per day than when either habit is sustained alone (Hirayama 1986). Animal experiments have demonstrated that ethanol can increase the carcinogenicity of nitrosamines (components of tobacco smoke) (Driver and Swann 1987). Other studies have indicated that alcohol leads to enhanced microsomal activation of carcinogens and mutagens (Lieber et al. 1979) and that alcohol itself may act as a cocarcinogen. It has also been reported that alcohol-fed rats have deficient ability to repair a specific type of carcinogen-induced DNA damage that may promote development of precancerous lesions (Garro et al. 1986). Alcohol is also associated with dietary deficiency that may increase cancer risk; for example, vitamin A deficiencies are associated with respiratory tract cancer in rats (Driver and Swann 1987).

Alcohol may also play a role in carcinogenesis through its effects on the immune system (see section on immune system) by decreasing immune surveillance against tumors, particularly by means of suppressor and cytotoxic T-lymphocytes.

In summary, alcohol may both facilitate and promote delivery of carcinogens and then impair immune protective or repair mechanisms, although more research is needed to test these hypotheses. Evidence strongly suggests an association between chronic alcohol consumption and some types of cancer, but the relationship is complex.

Effects on Endocrine and Reproductive Functions

Alcohol affects virtually every endocrine organ. The effects vary with dose and with whether determinations are made after acute or chronic administration or withdrawal. Nutritional state and stress associated with alcohol administration are also important variables. Alcohol-induced hormonal changes alter metabolism and predispose to organ damage and may also mediate physical dependence and tolerance.

Elevated plasma cortisol levels have been found in alcohol-dependent individuals, and some have pseudo-Cushing's syndrome—in which corticosteroids are increased while adrenocorticotropic hormone levels are normal—suggesting possible adrenocortical disturbance (Ylikahri et al. 1978; Rees et al. 1977). The abnormalities disappear after 2 to 3 weeks of abstinence.

The specific effects of alcohol use on the mechanisms responsible for regulating corticosteroid levels are not clear, but the decisive events may occur (a) at the level of the pituitary gland, the producer of adrenocorticotropic hormone (ACTH), which stimulates the adrenal cortex to secrete the cortical steroids, or (b) higher up, in the brain, where the hypothalamus produces corticotropin-releasing factor, a substance that signals the pituitary to release ACTH. In animals, chronic alcohol administration causes enlargement of the adrenal glands and increases circulating cortisol levels. These effects are prevented by removing the pituitary gland (hypophysectomy) (Crabbe and Rigter 1980). Acute alcohol administration consistently increases plasma corticosteroids, an effect that appears to be mediated at the brain level because it is blocked when the pituitary gland is removed (Crabbe and Rigter 1980). A direct adrenal effect is also possible, however, because ACH increases hormone synthesis and secretion by the isolated perfused adrenal gland (Cobb and Van Thiel 1982; Cobb, Van Thiel, and Gavaler 1981; Cobb, Van Thiel, Gavaler, and Lester 1981; Cobb et al. 1979).

Plasma catecholamines are increased by acute alcohol administration, as demonstrated by studies in which alcohol infusion raised adrenal vein output of epinephrine and norepinephrine (Koob 1983). Chronic alcohol administration increases the rate at which adrenal catecholamines are depleted and replaced, and recent studies have found that chronic alcohol feeding decreases the density of alpha-1-adrenergic receptors in plasma membranes. Liver adrenergic receptors are predominantly of this subtype, and it is through these receptors that epinephrine affects mitochondrial respiration, intracellular calcium, and carbohydrate metabolism (Gardemann et al. 1989). Bjorneboe et al. (1988) found lower levels of serum calcium levels in alcohol-dependent individuals compared to controls when dietary intake of vitamin D3 was not significantly different, indicating that the activities of enzymes crucial in vitamin D3 metabolism may be altered in alcohol-dependent individuals.

Other endocrine effects include alterations in thyroid hormones, growth hormone, and vasopressin (Hegedus 1984). Patients with alcoholic hepatitis and cirrhosis have decreased triiodothyronine levels but normal thyroxine levels and normal or increased levels of thyroid-stimulating hormone. The decreased triiodothyronine correlates with the severity of the liver disease (Van Thiel et al. 1979). In a study of patients with nonalcoholic and alcoholic cirrhosis, Hegedus et al. (1988) found decreased thyroid size in patients with alcoholic cirrhosis but not in those with nonalcoholic cirrhosis, suggesting that alcohol may have a toxic effect on the thyroid gland independent of the degree of liver damage.

It is well known that disorders of reproductive function (including impotence, low testosterone levels, low sperm count, and testicular atrophy) are common among alcoholic men (Cicero 1982; Noth and Walter 1984; Van Thiel 1983). Breast enlargement has also been observed clinically in alcoholic men and may be associated with elevated levels of prolactin or perhaps estrogen. Episodic heavy drinkers also may have alcohol-related impotence and low testosterone, and there is some evidence that alcohol may impair spermatogenesis (Van Thiel 1983; Van Thiel et al. 1974).

Although there is now considerable evidence that alcohol directly affects testosterone production in the testes (Ellingboe and Varanelli 1979; Gordon et al. 1980; Chiao et al. 1981; Johnston et al. 1981), the cellular mechanisms involved are not understood. Controversy also persists concerning the extent to which the hypothalamus and pituitary are affected simultaneously by alcohol to modulate the suppressive effect on testosterone production. Adding to the complexity is evidence that cortisol can act directly to reduce testosterone levels (Cumming et al. 1983).

Most clinical and endocrine studies of alcohol have been carried out in men. The few clinical studies of alcohol-dependent women suggest that they have higher prevalence of amenorrhea, anovulation, dysfunction in the postovulation phase of the menstrual cycle, and pathologic ovary changes (Hugues et al. 1980; Moskovic 1975; Valimaki et al. 1984), and perhaps accelerated onset of menopause as well (Gavaler 1985). Mendelson et al. (1987) found significant effects of alcohol on female hormone secretion when controlling for the phase of the menstrual cycle. The findings indicate that repeated or sustained episodes of alcohol intoxication may suppress hormonal activity in women. In a detailed study of the relationship between alcohol intoxication and the menstrual cycle, Sutker et al. (1987) found differences in alcohol metabolism across different phases of the menstrual cycle among women who had ovulated during two previous cycles.

Neurologic Disorders

Heavy alcohol consumption is a well-documented cause of brain damage (Lee et al. 1979; Carlen et al. 1986). Neurological complications of heavy alcohol consumption include dementia, blackouts, seizures, hallucinations, and peripheral neuropathy (Miller and Gold 1987);

in addition, other factors may contribute to behavioral impairment in chronic alcohol-dependent individuals. Alcohol-related dementia accounts for nearly 20 percent of all admissions to state mental hospitals (Freund and Ballinger 1988). Upon neuropsychological assessment, there is evidence of brain dysfunction in 50 to 70 percent of detoxified alcohol-dependent individuals who do not have organic brain syndrome (a constellation of psychological signs and symptoms associated with a specific organic cause) (Eckardt and Martin 1986). Structural brain damage in alcohol-dependent individuals, which can be seen on autopsy, includes general atrophy as well as specific cell loss in at least two structures associated with memory disorders (Butters and Cermak 1983). Freund and Ballinger (1988) found that heavy alcohol consumption was associated with loss of a specific type of acetylcholine receptor in the frontal cortex. This loss could disrupt synaptic transmission of nerve impulses and thereby cause varying degrees of impaired memory and learning.

Investigations of neurologic damage associated with long-term alcohol use that include the use of computerized tomography (CT) scans have revealed structural abnormalities that correlated with results on neuropsychological tests (Harper and Kril 1985). From 50 to 75 percent of detoxified, long-term alcohol-dependent individuals show significant impairments in tests of problem solving, perception, and memory. Many of these alcohol-dependent individuals have demonstrable brain abnormalities—a widening of the frontal and parietal cortical sulci (furrows separating brain convolutions) and often a widening of the lateral and third ventricles of the brain (Pfefferbaum et al. 1988; Bergman 1987; Wilkinson and Carlen 1980; Carlen et al. 1981).

Correlations have also been found between the size of the third ventricle, which includes the dorsomedial thalamic region, and paired-associate learning tasks (Gebhardt et al. 1984). There is a consistent trend toward more neuropsychological deficits in general intelligence, verbal learning and retention, and short-term memory in those with wider lateral ventricles (Bergman 1987). However, this trend is more pronounced in middle-aged or older alcohol-dependent persons (Bergman 1987). Pfefferbaum et al. (1988) found that ventricular enlargement was apparent only in older alcohol-dependent individuals and became increasingly exaggerated with age, although enlargement of the sulci was found in all age groups. However, associations between neuropsychological performance and CT changes or alcohol consumption were not very pronounced.

Evidence suggests that in some alcohol-dependent persons hepatic disease may mediate some of the neuropsychological impairment. The performance of alcohol-dependent individuals with cirrhosis on most neuropsychological tests does not differ substantially from that of non-alcohol-dependent individuals with cirrhosis, and certain liver enzyme and function indices correlate significantly with neuropsychological test scores (Tarter and Edwards 1986; Tarter et al. 1986). The 45-percent incidence of hepatic encephalopathy in alcohol-dependent individuals with hepatitis suggests that cognitive impairments may be apparent before the stage of cirrhosis (Tarter and Edwards 1986). Furthermore, lactulose (a drug used to treat portal-systemic encephalopathy) can partially attenuate the neuropsychological deficits in alcohol-dependent individuals (Tarter and Edwards 1986). In a recent study, Tarter et al. (1988) found no systematic differences on neuropsychological tests between alcohol-dependent individuals and non-alcohol-dependent individuals, all of whom had biopsy-proven cirrhosis, and concluded that a history of alcohol dependence does not contribute substantially to the manifest neuropsychological deficits beyond the deficit due to coexistent hepatic encephalopathy.

There also is some evidence that abstinence may lead to recovery of some cognitive function and learning and partial recovery from brain atrophy (Goldstein et al. 1968; Goldman 1982; Carlen et al. 1986; Ron 1983) and significant reduction in brain abnormalities as seen on CT scans (Carlen et al. 1978; Artmann et al. 1981; Ron et al. 1982; Cala et al. 1983; Carlen et al. 1986). Abstinent alcohol-dependent individuals under age 40 have been observed to recover visuospatial capacity more frequently than older abstinent alcohol-dependent individuals (Goldman et al. 1983). However, another study found that a 5-year abstinence in young alcohol-dependent individuals permitted some perceptual recovery but did not reverse memory and learning deficits (Brandt et al. 1983). Other studies of detoxified or recovering alcohol-dependent individuals confirm some long-term cognitive deficits (Yohman et al. 1985; Fabian and Parsons 1983). Such deficits may have implications for treatment and relapse; particularly in the first weeks of abstinence during treatment, cognitive impairments may make it difficult for some alcohol-dependent individuals to benefit from the educational and skill-development sessions that are important components of many treatment programs (see chapter XI).

The relationship between different behaviors and anatomical changes in the brain is not yet completely clear, however. The pattern of deficits is not always the same, and up to 25 percent of chronic alcohol-dependent individuals have no cognitive deficits upon neuropsychological assessment (Tarter and Edwards 1986). CT studies that have found correlations between brain structural changes and behavior in alcohol-dependent individuals have involved both cortical and subcortical structures. A major problem in determining correlations is the limited resolution of CT scans, which seriously restricts the ability of investigators to examine alterations in subcortical structures. Newer technologies such as magnetic resonance imaging are far superior to CT scans in revealing details of brain structure because they allow volumetric analysis of subcortical structures (see fig. 6).

A study comparing female alcohol-dependent individuals with no overt clinical evidence of brain damage to a female nonalcoholic control population (Jacobsen 1986) found that female alcohol-dependent individuals had larger ventricles and greater degrees of widening of sulci and fissures than the controls. Perhaps of most significance in this study (as compared to CT studies in male alcohol-dependent individuals), female alcohol-dependent individuals had markedly shorter histories, lower levels of "peak" alcohol consumption, and substantially shorter durations of withdrawal symptoms than were usually reported for male alcohol-dependent individuals. Thus the pattern of CT abnormalities similar to those found in males appeared after significantly shorter and less intense drinking histories; this pattern is consistent with findings for other alcohol-induced organ damage such as liver disease (Gallant 1987).

Results differ concerning the presence and extent of cognitive or structural damage associated with moderate alcohol consumption; some CT scans of the brain show such structural damage (Cala et al. 1978; Cala 1985) and others do not (Bergman et al. 1983). Findings concerning cognitive deficits associated with moderate alcohol use are also inconsistent (Parker et al. 1983; Parsons 1986; MacVane et al. 1982).

Brain impairment in chronic alcohol-dependent individuals may be conceptualized as two organic brain syndromes: alcoholic dementia and Korsakoff's psychosis (Wernicke-Korsakoff syndrome) (Martin et al. 1986). Alcoholic dementia is characterized by global intellectual decline with deficits in abstracting ability and problem solving, difficulty in swallowing (dysphagia), difficulty in manipulating objects (apraxias), electroencephalographic abnormalities, and cerebral atrophy and ventricular dilation on CT scans (Martin et al. 1986). These are considered to be direct effects of alcohol neurotoxicity, but they are sometimes difficult to differentiate from symptoms of primary degenerative dementia or Alzheimer's disease (Martin et al. 1986).

Wernicke's disease is a CNS disorder consisting of ocular disturbances, ataxia, and confusion. It is associated with thiamine deficiency and can be reversed by adequate thiamine intake (Martin et al. 1986). Korsakoff's psychosis may appear without being preceded by thiamine deficiency; when it does so, it is not reversed by thiamine supplementation. Alcohol-dependent individuals may have the syndrome or Korsakoff's psychosis alone. Approximately 80 percent of patients with Wernicke's encephalopathy who survive will have Korsakoff's psychosis (Reuler et al. 1985). Many investigators consider that Wernicke's encephalopathy and Korsakoff's psychosis are really the same disorder, with Wernicke's being the acute and Korsakoff's the chronic form (Thomson et al. 1987).

The etiology of this syndrome is complex; structural lesions have been demonstrated in the dorsomedial thalamic nucleus and the basal forebrain region (Victor et al. 1971; Wilkinson and Carlen 1981; Arendt et al. 1983). It has also been suggested that there may be a genetic predisposition to Wernicke's encephalopathy involving an enzymatic abnormality concerned with thiamine metabolism (Reuler et al. 1985; DeVor et al. 1988; Thomson et al. 1987; Martin et al. 1986). Recognizing the progressive nature of Wernicke's encephalopathy is vital because mortality is 10 to 20 percent and early treatment may correct critical abnormalities (Reuler et al. 1985).

Korsakoff's psychosis consists of a permanent state of cognitive dysfunction and the inability to remember recent events or to learn new information. For alcoholic patients with Korsakoff's psychosis, previously learned information may interfere with new learning, and it may also be difficult to recall events that occurred before the onset of the dysfunction (Butters 1984; Butters and Brandt 1985).

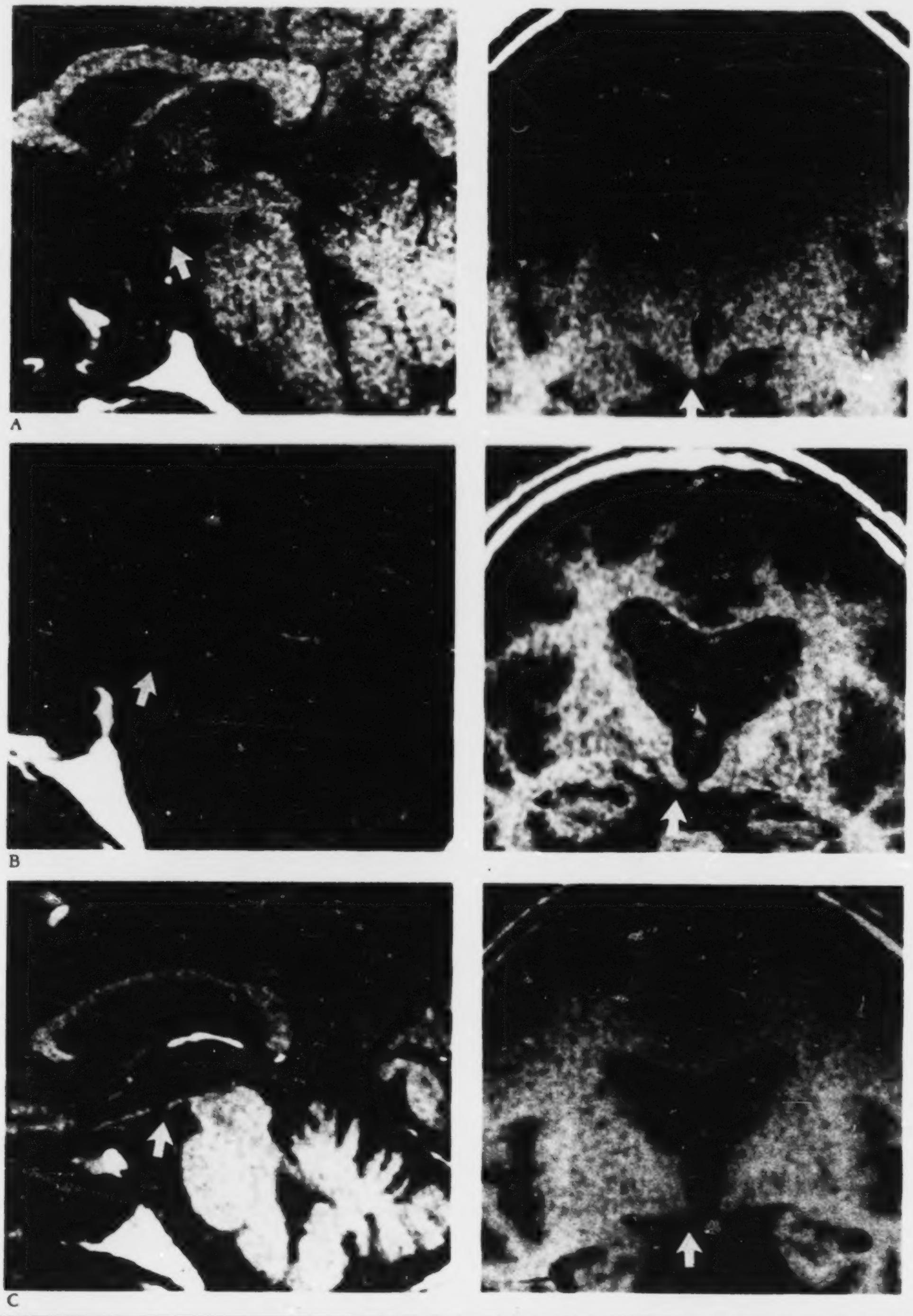

FIGURE 6. Magnetic resonance T_1-weighted brain scans through the plane of the mamillary bodies. Left and right are 1.7X enlargements of 3-mm-thick brain sections that are sliced sagittally (vertical cuts made with the knife in the front-to-back position) and coronally (vertical cuts made with the knife in the left-to-right position) respectively. (A) Normal control; (B) Alzheimer's disease; (C) chronic Wernicke's encephalopathy. The mamillary bodies, indicated with arrows, are easily seen in the control patient, only slightly smaller in the Alzheimer patient despite striking ventricular enlargement, and barely discernible in the Wernicke patient.
SOURCE: Charness and DeLaPaz 1987.

The relationship between alcoholic brain damage and behavior is an area ripe for more intensive research. Classic, long-accepted studies of alcohol neuropathology are now being criticized. For example, acute hemorrhagic lesions in the medial diencephalic region of the brain (an area that lies immediately behind the forebrain and includes upper portions of the hypothalamus and lower portions of the thalamus) have long been considered responsible for the persistent amnesia in Wernicke-Korsakoff syndrome, but a study of 200 alcohol-dependent individuals found that although 131 had the neuropathology associated with Wernicke-Korsakoff syndrome, only 20 percent of the 131 had any signs of the illness. The condition is recognized far more often at autopsy than during clinical examination (Cravioto et al. 1961; Harper 1979; Torvik et al. 1982).

Among other neuropsychological effects of alcohol abuse, one of the most well-recognized is seizures following abrupt withdrawal of alcohol. However, a recent study by Ng et al. (1988) suggests that seizures may be caused by alcohol use itself in addition to withdrawal. In a controlled study, the researchers investigated alcohol use before the onset of a first seizure in 308 patients with seizures. In this study, alcohol withdrawal was not associated with the onset of seizures; 16 percent of first seizures in drinkers fell outside the conventionally defined withdrawal period, and the remainder appeared to occur randomly after the last drink in those who were abstinent. The investigators concluded that the relationship of seizures to alcohol use is dose dependent and that ingestion of alcohol can induce seizures independent of alcohol withdrawal.

Additional psychopathology, such as depression or antisocial personality disorder, may be concurrent with alcohol dependence and influence psychological test results. Parker et al. (1987) found that increased quantity of alcohol consumed per occasion was associated with increased depression symptoms in the sober state. For additional discussion of depression and alcohol dependence, see chapter XI.

Summary

The range of medical consequences of alcohol abuse is both immense and complex—virtually no part of the body is spared the effects of excessive alcohol consumption.

Injury to the liver (the primary site of alcohol metabolism) is of three major types: fatty liver and alcoholic hepatitis, which may be reversible with abstinence, and cirrhosis, which is irreversible. Although mortality from cirrhosis has been steadily declining since 1973 for reasons that are not yet clear, chronic liver disease and cirrhosis was the ninth leading cause of death in the United States in 1986.

Patients with perivenular fibrosis at the fatty liver stage are more likely to progress to more severe stages of alcoholic liver disease if they continue to drink. At present, liver biopsy is the only reliable method of detecting PVF, but noninvasive tests are being developed.

Liver transplantation has been used successfully for alcoholic liver disease. In a major study of transplantation, survival rates did not differ between patients with end stage alcoholic liver disease and nonalcoholic controls.

In the gastrointestinal tract, regular alcohol consumption may precipitate esophagitis and exacerbate existing peptic ulcers. The relative risk of esophageal cancer is higher in alcohol abusers, as is the incidence of chronic atrophic gastritis, a precursor of gastric carcinoma. Heavy alcohol consumption is a principal cause of chronic pancreatitis and a common cause of acute pancreatitis.

Results of nutritional deficiencies, a frequent complication of alcohol dependence, include anemia, neuropathy, Wernicke's disease, and depressed cellular and hormonal functions. Nutritional deficiencies also may contribute to the fetal alcohol syndrome, liver disease, pancreatic disease, malabsorption, and carcinogenesis. Alcohol also has profound metabolic effects on carbohydrate, lipid, and protein metabolism.

Chronic alcohol abusers may develop clinical signs of cardiac dysfunction, and up to 50 percent of excess mortality in alcohol-dependent individuals and heavy users may be attributed to cardiovascular disorders. Alcohol can affect the heart muscle itself, producing cardiomyopathy (degeneration of the heart muscle) and cardiac arrhythmias. Chronic alcohol consumption is associated with a significant increase in hypertension and may play an important role in ischemic heart disease and cerebrovascular disorders, including stroke.

In addition to possible direct action on the heart, alcohol may alter circulatory function by affecting the release and actions of hormones and related substances, changes in which may alter cardiac activity, blood pressure, blood flow, and vascular homeostasis, and eventually may result in cardiac and vascular damage.

Alcohol also affects the immune functions and the endocrine and reproductive functions and may be associated with increased risk of certain kinds of cancers, especially those of the liver, esophagus, nasopharynx, and larynx. The well-documented neurological complications of heavy alcohol consumption include dementia, blackouts, seizures, hallucinations, and peripheral neuropathy.

As research on the mechanisms of alcohol-induced injuries proceeds, better understanding of how alcohol produces these effects is emerging. However, this picture is enormously complex, and it now appears that several diverse mechanisms may be involved. New concepts and technological advances have great potential to accelerate progress in understanding the biomedical consequences of alcohol dependence and in developing improved methods to treat and prevent the consequences of alcohol dependence and alcohol abuse.

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Chapter VI

Fetal Alcohol Syndrome and Other Effects of Alcohol on Pregnancy Outcome

Introduction

In 1973 a description of a common pattern of birth defects observed in children born to alcoholic mothers was published (Jones and Smith 1973; Jones et al. 1973). The distinct cluster of symptoms was labeled fetal alcohol syndrome (FAS). Since these initial reports, a great deal of clinical and basic research has ensued, firmly establishing alcohol as a teratogen (i.e., an agent that produces defects in offspring in utero). As a result of this research, it soon became apparent that the deleterious effects of in utero alcohol exposure exist on a continuum, ranging from gross morphological defects at one extreme to more subtle cognitive-behavioral dysfunctions at the less severe end. The latter effects have established alcohol as a behavioral teratogen.

With a preponderance of case reports accumulating, it also became apparent that minimal criteria needed to be established for diagnosing the syndrome: prenatal and postnatal growth retardation, a characteristic constellation of craniofacial anomalies, central nervous system (CNS) dysfunction, and major organ system malformations (Clarren and Smith 1978; Rosett 1980). Most recently, computer-assisted quantitative morphometric techniques have been employed to refine the diagnostic criteria for FAS (Clarren, Sampson, et al. 1987). Use of the term "suspected fetal alcohol effects" (FAE) has been recommended when only some of the criteria for FAS are met (Clarren and Smith 1978).

Both FAS and FAE represent major public health problems, with treatment costs for FAS in the United States estimated at nearly a third of a billion dollars per year (Abel and Sokol 1987; Sokol and Abel 1988). Moreover, prenatal alcohol exposure is one of the leading known causes of mental retardation in the Western world (Abel and Sokol 1986a). It is not surprising that a great deal of research has focused on characterizing the adverse effects of in utero alcohol exposure, as well as probing for underlying mechanisms.

This chapter is a selective review of recent research reports on the effects of maternal alcohol consumption on pregnancy outcome, with particular emphasis on important current work. Both clinical and animal research findings are presented as they relate to FAS as well as to FAE. Because details of earlier reports on FAS and FAE were presented in the *Sixth Special Report to the U.S. Congress on Alcohol and Health* (USDHHS 1987), these older reports are cited here only if they relate to newer findings.

Early estimates of the incidence of FAS were in the range of 1 to 3 cases per 1,000 live births (or an average of 1.1 per 1,000). Abel and Sokol (1987) surveyed 19 worldwide prospective and retrospective epidemiological studies on FAS frequency and calculated the incidence to be

1.9 cases per 1,000 live births (164 identified FAS cases out of 88,236 live births). Retrospective studies yielded higher rates than prospective studies (2.9 versus 1.1 per 1,000), and reported rates were higher in North America than in Europe and other countries (2.2 versus 1.8 per 1,000).

In addition to the method by which alcohol intake is ascertained (prospective versus retrospective approaches), the study population also causes great variance in the prevalence of FAS. For example, when one considers only the population of heavy-drinking (alcohol-dependent) women, the incidence rate may be as high as 25 per 1,000 live births (Abel 1984). Furthermore, most identified cases of FAS in the United States have come from study sites where the mothers were black or American Indian and of low socioeconomic status. The estimated rate at these sites was 2.6 per 1,000 compared to 0.6 per 1,000 from other study sites where the mothers were white and of middle socioeconomic status.

As expected, given the less restrictive criteria, the incidence of FAE is estimated to be much higher than FAS. Among the general population, Abel (1984) estimated the incidence of FAE to be approximately three times greater. The difference was nearly fourfold in the alcohol-abusing population.

Clinical Studies

Followup Studies of FAS Children

At 3 to 4 years after the original diagnosis of 72 FAS cases in Germany (Steinhausen et al. 1984), various subgroups of these children were reexamined (Spohr and Steinhausen 1987). The patients underwent pediatric, neurological, and psychiatric assessments; electroencephalograph (EEG) recordings; and psychological testing. Pediatric reexamination of 54 children from this cohort revealed significant improvements in craniofacial dysmorphology, muscular hypotonia, and morphometric measures of length, weight, and head circumference. In addition, neurologic performance improved and EEG patterns in 45 children were more normal than their original recordings. These improvements could not be explained by social background, therapeutic measures, sex, or age.

Psychiatric assessment of 28 children at approximately 8 years of age involved a structured interview, and symptoms were rated and combined to yield an overall psychopathology score. Although there was some improvement in the overall score, FAS children still scored higher than a control group matched for age, sex, and socioeconomic status (Steinhausen et al. 1984). Improvements were noted in several categories including clumsiness, impaired concentration, difficulties with siblings, temper tantrums, negative mood, and phobias. However, other problematic symptoms persisted, such as hyperactivity, abnormal habits, speech disabilities, and anxiety. Finally, psychological testing revealed some improvement on the Columbia Mental Maturity Scale. However, the authors cautioned that only some children with subnormal intelligence (IQs of 70 to 85) have improved. The more severely retarded children (IQs of less than 70) showed no signs of improvement or were too handicapped to participate in the test (Spohr and Steinhausen 1987). Although improvement was noted on several levels in this study, particularly those related to physical appearance, cognitive deficiencies were the most striking features that persisted: the authors reported that a remarkably high proportion of the study population required special educational training. Moreover, the study revealed that the positive correlation between degree of mental disability and physical dysmorphology noted in children initially diagnosed with FAS persisted over time.

Identifying High-Risk Factors for Fetal Alcohol Syndrome

Although FAS has not been reported in children of "social-" or "moderate-" drinking women, it has become increasingly apparent that not all women who drink alcohol excessively during pregnancy will deliver babies with FAS or even FAE. In fact, far fewer cases of FAS and FAE have been reported relative to the frequency of abusive drinking in pregnant women. For example, among 204 women identified as alcohol abusers (out of more than 12,000 examined in a large-scale epidemiological study), only 5 (2.5 percent) gave birth to children diagnosed with FAS. Moreover, when FAE were considered, only 50 percent of the children born to alcohol-abusing women evidenced adverse effects attributable to prenatal alcohol exposure (Sokol et al. 1980). Similarly, a study on infant neurobehavioral development revealed that only 5 to 10 percent of the infants born to women categorized as "heavier" drinkers during pregnancy (at least four standard drinks per day) scored abnormally low on mental and psychomotor scales at

8 months of age (Streissguth et al. 1980). In addition to these clinical reports, animal research has indicated variable susceptibility of fetuses to alcohol's adverse effects despite presumably similar levels of exposure.

Other factors in conjunction with the amount of alcohol intake may influence vulnerability to alcohol's teratogenic actions. It is conceivable that a number of factors, including genetic and maternal variables, may explain why some infants are spared while others are damaged by heavy drinking during pregnancy. For example, the increased susceptibility of blacks to the deleterious effects of prenatal alcohol exposure has been demonstrated in epidemiological studies (Chavez et al. 1988; Iosub et al. 1985). However, given the ubiquity of FAS reports throughout the world, it is clear that no ethnic or racial groups are immune to the teratogenic actions of alcohol. Nevertheless, additional research aimed at identifying factors that may place the fetus at greater risk for FAS or FAE are certainly warranted (Abel and Sokol 1986b; Sokol and Abel 1988). The information gained from such studies undoubtedly will aid in the task of more specifically targeting prevention and intervention strategies to those individuals falling into high-risk categories for FAS.

Another approach to this issue is to develop better screening techniques for identifying women who are at high risk for abusive alcohol consumption throughout their pregnancy. While many women spontaneously reduce their alcohol consumption during pregnancy, others continue to overindulge (Fried et al. 1980; Little and Streissguth 1978; Weiner et al. 1983). A study was conducted to determine whether women who drink throughout pregnancy can be differentiated from those who discontinue alcohol use sometime during their pregnancy (Smith et al. 1987). Of the 267 pregnant women interviewed (primarily during the second trimester), 121 reported abstinence from alcohol during pregnancy and were classified as nondrinkers. Based on interviews conducted within 3 days after delivery, approximately two-thirds of the remaining drinkers (96 out of 146) reported continuing to use alcohol throughout pregnancy despite having received information about the harmful effects of prenatal alcohol exposure. Analysis of data collected from the prenatal interviews revealed that women who continued to drink and those who discontinued alcohol use did not differ in age, marital status, number of previous pregnancies, cigarette and caffeine consumption, amount of alcohol consumed per week (which ranged from 1 to 75 ounces of absolute alcohol), and use of other drugs. However, the two groups did differ on a number of other parameters. The best predictors of continued drinking throughout pregnancy were the length of drinking history, reported tolerance to alcohol, a history of alcohol-related illness, and a preferred social context of drinking with other family members.

These results suggest that a number of biological (i.e., medical) and behavioral factors may be useful for identifying women at greater risk for continued alcohol abuse throughout pregnancy. The importance of identifying and targeting these high-risk women for intensive prevention efforts is perhaps best underscored by the fact that pregnancy outcome was found to be significantly compromised—that is, there was greater frequency of intrauterine growth retardation, dysmorphology, and neurobehavioral alterations—in women who continued to drink throughout pregnancy in comparison to the nondrinkers and those who discontinued drinking sometime during pregnancy (Coles et al. 1985, 1987; Smith et al. 1986).

Sokol and his colleagues developed a simple and brief questionnaire appropriate for detecting heavy alcohol drinking in pregnant women (Sokol et al. 1989). The test instrument, referred to as T-ACE (from the four test questions pertaining to alcohol *t*olerance, *a*nnoyance by criticism, *c*utting down, and *e*ye openers), was found to identify correctly 69 percent of the "risk drinkers" (defined as consuming 1 ounce of absolute alcohol per day) out of a cohort of 971 pregnant women. Moreover, the T-ACE test was found to be superior to other standard instruments used for detecting alcohol abuse, such as MAST and CAGE tests (see chapter VIII), in identifying risky drinking behavior. Because the test is brief, the investigators suggested that it may be a useful screen that can be easily administered in prenatal clinics and obstetrics and gynecology offices. Data on pregnancy outcome in this cohort will be required to further link the identified maternal risk factor to infant outcome. Nevertheless, pending further validation with other sample populations, broad application of this test might significantly contribute to better risk identification, appropriately targeted prevention efforts, and improved pregnancy outcome.

Effects of Lower Levels of Alcohol Drinking During Pregnancy

With the accumulation since 1973 of a large number of case reports on children with FAS, it has become apparent that these severely affected children are born to only those mothers who consume large amounts of alcohol daily during pregnancy. However, it is now generally accepted that the adverse effects of prenatal alcohol exposure exist on a continuum, with the complete FAS representative of one extreme and incomplete features of FAS, including more subtle cognitive-behavioral deficits, existing on the other end of the spectrum. Thus attention also has been focused on the effects of more moderate drinking on pregnancy outcome.

However, because the effects of lower levels of maternal drinking during pregnancy are more subtle and variable, as well as more neurobehavioral than physical, they are more difficult to detect and attribute to in utero exposure. This difficulty has necessitated the use of prospective longitudinal studies involving large sample populations and sophisticated statistical treatment of data to control for a variety of lifestyle factors.

One such study has been the ongoing Seattle Pregnancy and Health Study (Streissguth et al. 1981). In this longitudinal study, 1,529 women were given structured interviews during the fifth month of pregnancy about their alcohol, tobacco, and other drug use, as well as about a variety of other lifestyle characteristics. Of this large sample, a cohort of approximately 500 children born to these mothers were selected for followup analysis at birth, 8 and 18 months of age, and 4 and 7 years of age. Followup studies have now been completed through age 7. The relatively high rate of followup in this large-scale longitudinal study was achieved by extensive outreach activities.

The mothers of this cohort were primarily white (87 percent), married (86 percent), and middle class (81 percent). The average maternal age during pregnancy was 26, and 86 percent of the mothers had graduated from high school. The self-reported levels of alcohol consumption varied widely, and the group was stratified into three levels according to the amount of alcohol consumed during pregnancy and in the weeks before recognition of pregnancy. Alcohol consumption was expressed as the average daily intake of absolute alcohol, and the three levels of maternal drinking were defined as light (less than 0.1 ounce per day), moderate (0.1 to 0.9 ounces per day), and heavy (1 ounce or more per day). For the cohort that was studied at 7 years of age, light, moderate, and heavy maternal drinking patterns represented 49, 32, and 19 percent of the sample population, respectively. Twenty-seven percent were total abstainers, whereas 5 percent of the mothers reported drinking at least 2 ounces of absolute alcohol per day.

The most recent findings from the Seattle longitudinal study (Streissguth et al. 1986) indicate that the effects of heavy maternal alcohol consumption during pregnancy endure in children in their school-age years. Children from the original cohort were given a computerized continuous performance test (CPT). This vigilance task requires the subject to respond by pressing a button immediately after the letter "X" is displayed on a screen. A more difficult phase of the test requires the subject to respond to the presentation of the letter "X" only where preceded by the letter "A." As a measure of distractibility, the ability to perform the task while the computer generated clicking sounds was periodically assessed as well. Prenatal alcohol exposure was found to be related significantly to increased CPT errors of commission (responding at inappropriate times) and slower reaction times. Children of the heavier-drinking mothers were also more likely to be distracted by the computer-generated noises (Streissguth et al. 1986). These persistent attentional decrements, distractibility, and slower reaction times may have ramifications with regard to classroom learning.

In all phases of this longitudinal study, alcohol-related effects were identified after statistical analyses were conducted to adjust for a variety of covariates including other drug exposures, postnatal conditions, and demographics. In addition, while children of the heavier-drinking mothers were most affected (they showed measurable decrements in performance on attention and vigilance tasks at ages 4 and 7), these children were otherwise clinically normal. However, the investigators clearly cautioned against premature generalizations and interpretation of these results for several reasons. First, information on the amount of alcohol consumed was obtained by self-report and thus represents only a general estimate of actual exposure. Although these self-reports may be considered fairly accurate because the women were interviewed at a time when there was no information available about moderate drinking and pregnancy outcome (1974–75), it is important to recognize that the measures of estimated daily alcohol intake were averaged across a variety of drinking patterns, both between and within individual women. Second, the neurobehavioral decrements noted in these children were relatively small and therefore required a large sample size to achieve statistical significance. Third, the findings of this study pertain to children tested under laboratory conditions; the significance of these deficits for the individual child in natural settings is difficult to assess at present. Finally, future studies will need to address how long these attentional deficits persist and if they do in fact hamper classroom learning and school performance.

Other studies have reported similar neurobehavioral deficits and intrauterine growth retardation in infants born to mothers who were moderate consumers of alcohol during pregnancy (Coles et al. 1985; Little et al. 1986). Coles et al. (1987) examined whether abstaining from alcohol during the second trimester would improve pregnancy outcome. As part of a longitudinal research project, women applying for prenatal care at an inner-city hospital in Atlanta (serving a predominantly black and lower socioeconomic population) were screened for alcohol use. The mothers included those who never drank during pregnancy, those who drank an average of approximately 14 ounces of absolute alcohol a week (roughly four standard drinks per day) throughout pregnancy, and those who drank the same amount but quit by the second trimester. Healthy, full-term infants born to these mothers were examined for behavioral alterations at 3, 14, and 30 days of age using a standard infant assessment scale (Brazelton Neonatal Behavioral Assessment Scale).

None of the babies evidenced growth retardation, dysmorphic features, or any other signs of FAS. However, infants who had been prenatally exposed to alcohol had suboptimal neurobehavioral responses in comparison to infants who had not been prenatally exposed to alcohol. This finding was true of infants whose mothers had quit drinking by the second trimester and of infants whose mothers drank throughout pregnancy. However, the infants whose mothers had continued drinking into the second trimester scored significantly lower on tests of orientation toward visual and auditory stimuli, motor performance, and autonomic regulation. Some of these effects in the continuously exposed infants may have been related to neonatal alcohol withdrawal during the first few days of life (Coles et al. 1984), but a followup examination at 30 days of age revealed persistent behavioral alterations in these infants. In contrast, the infants who had not been exposed to alcohol since the end of the first trimester showed more recovery of reflexive behavior and autonomic control during those 30 days. These findings are consistent with the view that moderate prenatal alcohol exposure throughout gestation that does not result in physical abnormalities can have negative effects on behavior that are evident at, and persist beyond, birth.

However, many of the previously mentioned caveats may be applied to these studies as well, and so it has been difficult to gauge clinically the impact of low-level maternal drinking on pregnancy outcome. In particular, since all these studies rely on self-reported alcohol usage and the data are typically averaged over a period of a week or more (masking different drinking patterns), it is not possible to identify a particular level of social or moderate drinking during pregnancy that will not confer some degree of risk to the unborn child.

Critical Periods And Threshold Doses

Given the compelling evidence for alcohol's status as a teratogen, it is not surprising that issues pertaining to critical periods of exposure and threshold doses have been of great concern to both scientists and the public. However, questions such as How much alcohol is too much? and When is the fetus at greatest risk? or conversely, What level of alcohol drinking is safe? and When is the unborn child less likely to be affected? have proven difficult to address in clinical studies. Although some studies have begun to address these issues (Ernhart et al. 1987), the major problem with such studies stems from the lack of a specific physiologic measure that accurately reflects alcohol consumption.

This problem is not unique to the area of fetal alcohol research. Indeed, there is no such biological marker available for the measurement of alcohol intake in the general population. Because of the relatively short biological half-life of alcohol and the infeasibility of repeated blood sampling, clinical investigations have had to rely on self-reports of alcohol intake. Moreover, as public awareness increases about the dangers of drinking during pregnancy, the veracity of these self-reports may be questionable because of psychological denial and guilt. When quantitative reports of alcohol use obtained during pregnancy were contrasted with retrospective reports obtained 5 years later, marked discrepancies were found suggesting significant underreporting during pregnancy, and particularly so for women whose alcohol problems were identified through a screening instrument (Ernhart et al. 1988;

Morrow-Tlucak et al. 1989). Thus underreporting of alcohol use in pregnancy represents a real concern, particularly with regard to the establishment of related risk levels.

Some researchers have attempted to deal with this problem by framing the questions about alcohol drinking in a manner that does not trigger denial (Sokol et al. 1989) and by using a "bogus pipeline" technique in which the patient is led to believe that her behavioral self-report on alcohol use will be confirmed by a blood or urine test (Lowe et al. 1986). However, short of a physiological measure, the accuracy of self-estimates of alcohol intake, particularly during pregnancy, remains problematic with regard to assessing threshold levels and critical periods of fetal risk. For these reasons, along with others yet to be described in this chapter, the use of animal models appears to offer a distinct advantage for studying FAE and, in particular, issues pertaining to critical periods and threshold doses.

Indeed, animal research has shown that different profiles of alcohol-related birth defects are related to critical periods for specific aspects of fetal development (Randall 1987). In fact, as is the case with other classic teratogens, the nature of the birth anomalies appears to be not so much related to the teratogen itself as to when the pharmacologic or toxicologic insult occurs during fetal development. Thus it perhaps is not surprising that heavy chronic alcohol consumption throughout pregnancy results in a wide variety of effects ranging from structural anomalies to growth retardation (collectively characteristic of FAS). On the other hand, episodic binge drinking at high levels results in partial expression of the syndrome, with the abnormalities being unique to the period of exposure.

Critical dosages or exposure levels have been much more difficult to establish. Given the enormous range of defects that result from prenatal alcohol exposure, a unitary level of fetal risk may be unreasonable. That is, different aspects of development may be sensitive to different levels of exposure. As expressed by Clarren, Bowden, and Astley (1987, p. 345), "It is probable that there is no single dose-response relationship for ethanol teratogenesis, but rather that each abnormal outcome in brain structure or function, morphology, and growth has its own dose-response and gestational timing parameters."

Moreover, recent studies with rats have suggested that peak blood alcohol levels, rather than the amount of alcohol consumed per se, represent the "critical dosage" factor. West and his colleagues showed that the degree of alcohol-induced microencephaly was dependent on the pattern in which alcohol was administered (Pierce and West 1986a,b). That is, brain growth was significantly retarded when alcohol was administered to rat neonates (at a time corresponding to their brain growth spurt period) in a condensed fashion, so that blood alcohol levels cycled with high peaks (270 milligrams per deciliter). However, a minimal effect on brain growth was observed when the same dose of alcohol was spaced over a longer period of time so that blood alcohol levels were low (46 milligrams per deciliter) and stable with time. Similarly, a pattern of alcohol administration that resulted in high peak blood alcohol levels was found to result in the greatest functional (behavioral) deficits (Goodlett et al. 1987; Kelly et al. 1987, 1988).

These results have important clinical implications with regard to establishing relevant thresholds for humans. A host of factors can influence blood alcohol levels in both the mother and the fetus. For example, higher blood alcohol levels are achieved following episodic or binge drinking, particularly if alcohol is consumed on an empty stomach rather than after a meal. Thus, given the large number of variables that impact on the pharmacokinetics of alcohol (including individual differences in alcohol distribution and metabolism), identifying and demarcating a critical exposure level for the wide range of alcohol's teratogenic actions may be an unrealistic goal. It is nevertheless still important to identify and investigate maternal and fetal risk factors that render some individuals more susceptible than others to the deleterious effects of prenatal alcohol.

Research on the Effects of Prenatal Alcohol Exposure in Animal Models

Since the "formal" identification of FAS in 1973 (Jones et al. 1973), interest in developing and studying animal analogues of the clinical situation under laboratory conditions has increased, giving rise to a thriving area of research. Animal research has played a major role in advancing our knowledge of the myriad detrimental consequences that follow prenatal alcohol exposure.

Most importantly, the use of animal models has firmly established the teratogenic actions of alcohol by controlling for other potentially confounding variables, such as malnutrition, poor rearing (environmental) conditions, disease, smoking, and other drug use. In fact, under controlled laboratory conditions, alcohol-related birth defects have been demonstrated in a number of species including chickens, mice, rats, guinea pigs, dogs, and monkeys.

In some cases, findings generated from animal laboratory studies have helped guide clinicians in identifying defects previously not documented in children of alcohol-dependent mothers. For instance, renal defects were first observed in mice prenatally exposed to alcohol (Randall et al. 1977). After that report, kidney anomalies were searched for and found in children with FAS (Debeukelaer et al. 1977). A similar sequence of events applies to the discovery of auditory impairments in FAS children (Church 1987).

In addition, using animal models to study the effects of in utero alcohol exposure has allowed for a more mechanistic level of analysis. For example, neuroanatomical and neurochemical substrates of observed behavioral abnormalities can be elucidated and studied more directly in animals, whereas such studies in humans are obviously limited for a variety of reasons, including ethical considerations. Similarly, animal models have been developed to examine biochemical events underlying the structural teratogenic effects of alcohol. With continued refinement of these animal model systems, more sophisticated issues related to the etiology of alcohol-related embryopathology are currently being addressed. These research efforts ultimately may contribute to the development of therapeutic interventions or prevention strategies.

For a variety of reasons (including economy), rodents have been the most commonly studied species. In fact, research with mouse and rat models has provided a wealth of information with regard to the immediate as well as long-term consequences of prenatal alcohol exposure. Moreover, in reviewing the literature, one is struck by the remarkable similarity in findings from research with rodent models and human clinical studies. Some of the more recent research findings are outlined in the following paragraphs.

Sensorimotor Effects

A variety of sensorimotor deficits have been identified in children with FAS. These include visual, auditory, vestibular, and motor coordination problems.

Visual System

Visual system anomalies are very common in FAS. Aside from the facial or morphologic malformations that comprise some of the craniofacial features used for FAS diagnosis (microphthalmia, ptosis, and short palpebral fissures), disorders of ocular muscle coordination and defects of several intraocular structures have been reported as well. Strabismus or esotropia (crossed eyes), optic nerve hypoplasia (a reduction in the number of optic nerve axons), and abnormal vasculature in the retina have been most frequently observed (Stromland 1987). All of these defects contribute to compromised visual acuity, typically myopia (nearsightedness). Although a similar pattern of ocular facial features has been obtained in animal models (Sulik and Johnston 1983), little attention has been given to the pathogenesis of these ophthalmologic abnormalities. In a recent preliminary study, a combination of autoradiographical, histological, and morphometric techniques was employed to study patterns of neural cell proliferation and death in the eyes of mouse embryos after alcohol exposure (Kennedy and Elliot 1986). A single high dose of alcohol (5.2 grams per kilogram of body weight), or saline, was administered intraperitoneally on day 13 of pregnancy (the critical period for ocular development in the mouse). At 24 hours after treatment, alcohol-exposed embryos evidenced an increase in neuronal cell death and cell loss in the retina, as well as a sevenfold increase in duration of the neuronal cell cycle in comparison to controls. At 48 hours after treatment, a 25- to 29-percent reduction in the thickness of the neuronal layer of the retina and a 16- to 30-percent reduction in the size of the eyeball were observed in alcohol-exposed embryos. In another study, the rate of myelination of optic nerve axons was shown to be retarded in rats whose mothers consumed alcohol during pregnancy (Samorajski et al. 1986). These results suggest that an increase in retinal cell loss along with impaired cell replication due to prolongation of the cell cycle and hypomyelination of optic nerve axons may contribute to the pathogenesis of ocular abnormalities seen in FAS.

Auditory System

At least one report suggests that the incidence of auditory problems might be quite high in FAS children (Church 1987). In that study, 90 percent of the 12 FAS children examined had some degree of hearing loss. It also appears that prenatal alcohol exposure can have negative impact at various levels of the auditory system. By measuring electrical activity in the brainstem in response to high-frequency clicking sounds, Church and Holloway (1984) found evidence of sensorineural hearing loss in rats prenatally exposed to alcohol. A followup study (Church 1987) showed that the processing of auditory information at the cortical level, as measured by cortical auditory-evoked potentials, was disrupted in rats prenatally exposed to alcohol in comparison to control offspring. These results have important clinical implications because good hearing is essential for normal speech and language development in children.

Vestibular and Motor Systems

A variety of vestibular and motor coordination problems have been associated commonly with FAS. For example, Marcus (1987) reported on five FAS children who showed signs of axial ataxia and kinetic tremor. These motor problems are typically indicative of a dysfunctional cerebellum (a part of the brain that controls motor coordination). In reviewing 16 human FAS autopsies, Clarren (1986) also reported that cerebellar dysgenesis was found in 10 of the cases.

In an attempt to develop an animal model that approximates the motor dysfunctions observed in FAS children, Hannigan and Riley (1988) investigated the effects of prenatal alcohol exposure on the integrity of walking gait in rats. The investigators placed black ink on the hindpaws of the offspring and then had them walk down a paper-lined runway. Measures of stride length, stance width, step angle, and gait symmetry were taken from the footprints. The results indicated that adult rats whose mothers had consumed alcohol as 35 percent of their total calories during pregnancy exhibited a decrease in gait symmetry in comparison to control rats whose mothers consumed the identical number of calories during pregnancy, but no alcohol. These results are similar to previous studies in which rats prenatally exposed to alcohol exhibited greater motor incoordination and delayed development of motor reflexes (Abel and Dintcheff 1978; Lee et al. 1980). All of these effects resemble the motor dysfunctions that occur after disruption of cerebellar maturation, and prenatal alcohol exposure has been shown to have a deleterious effect on cerebellar development (Mohamed et al. 1987; Nathaniel et al. 1986; Phillips 1986). Whether the motor defects observed in animals prenatally exposed to alcohol are, in fact, related to altered cerebellar morphology requires further study.

Neonatal Behavioral Effects

Fetal Movement

Although the pernicious effects of prenatal alcohol exposure have been well characterized in offspring after birth, very little is known about how fetuses respond to alcohol in the womb. However, a procedure that allows direct observation of rat fetuses in utero has been employed to study the effects of alcohol administered to the mothers (Smotherman et al. 1986). Rats were intubated with alcohol or saline on the 19th day of pregnancy or received daily intubations on gestation days 15 to 19. Four hours after intubation on the 19th day of gestation, a cesarean section was performed and the mother's uterus was externalized and allowed to float in a warm water bath so that fetal activity could be observed. A single intubation of 4 grams of alcohol per kilogram of body weight produced a 51-percent reduction in overall fetal activity. The fact that behavioral suppression was observed after chronic alcohol exposure (five daily intubations) suggests that the fetal response to alcohol shows no signs of adaptation or tolerance. These results provide the most direct evidence that maternal ingestion of alcohol influences fetal behavior in utero. They also are consistent with a study indicating altered human fetal "breathing movements" monitored indirectly in mothers who had just consumed alcohol (McLeod et al. 1983).

Suppressed fetal movement also has been associated with shortened umbilical cord length. For example, human infants born with limb defects that restrict fetal movement also have shortened umbilical cords (Miller et al. 1981). Because prenatal alcohol exposure was found to reduce fetal activity in rats, these offspring would be expected to be born with shorter umbilical cords than controls. This prediction was, in fact, supported by a study in which the umbilical cords of fetal rats born to mothers who consumed alcohol during their pregnancy were found to be significantly shorter than the cords of control fetuses (Barron et al. 1986). This difference in umbilical cord length could not be attributed to differences in body weight.

Taken together, these results related to fetal activity, whether observed directly or inferred from umbilical cord length, have important implications because reduced fetal activity in utero has been shown to have profound effects on morphological development in animals and humans. For example, fetal inactivity resulting from congenital myopathy or neural dysfunction can cause physical anomalies and growth retardation (Moessinger et al. 1982). In addition, direct observation of fetal behavior revealed that the adaptive response patterns to brief, experimentally induced hypoxia were diminished in intensity and duration among fetuses exposed to alcohol in utero (Smotherman and Robinson 1987). Thus altered fetal activity as a result of in utero alcohol exposure may be a contributing factor in the etiology of FAS.

Feeding Behavior

Human infants prenatally exposed to alcohol have been characterized as poor feeders, exhibiting a weak sucking response and irregular sucking patterns early in life (Martin et al. 1979; Van Dyke et al. 1982). Chen et al. (1982) found that rat pups exposed to alcohol in utero took longer to attach to the nipple of a female than control pups. These findings have been extended by directly measuring suckling pressure in alcohol-exposed and control rat neonates (Rockwood and Riley 1986). As has been reported in human infants prenatally exposed to alcohol (Martin et al. 1979), rat pups exposed to alcohol in utero spent less time suckling and displayed weaker suckling pressure with an altered pattern of suckling in comparison to controls. These human and animal data suggest that inferior feeding behavior results from in utero alcohol exposure and in turn may contribute importantly to the postnatal growth retardation commonly seen in FAS and FAE offspring.

Temperature Regulation

The ability of a newborn to regulate its body temperature in a constantly varying environment is crucial for survival. Because infants with low birth weights appear to be exceptionally sensitive to fluctuating ambient temperatures (Avery and Taeusch 1984), and because low birth weight is a consistent hallmark of FAS (Clarren and Smith 1978), altered thermoregulation in babies born to alcohol-dependent mothers may contribute to the increased morbidity observed in this population. To examine this possibility, Zimmerberg and colleagues (Zimmerberg, Ballard, and Riley 1987; Zimmerberg, Beckstead, and Riley 1987) tested whether prenatal alcohol exposure impaired the ability of rat neonates to regulate their body temperature.

Pregnant rats were fed a liquid diet during pregnancy in which 35 percent of the calories were alcohol or, in the control situation, sucrose. A third group was fed standard rodent chow and water. Rat pups from each group were removed from their nests and placed in a temperature-controlled environment where their body temperatures were monitored for 4 hours. In a second experiment, the pups were tested for their ability to modulate their body temperature behaviorally. Thermotactic behavior was assessed by placing the pups on a walkway that was differentially heated to produce a temperature gradient from one end to the other.

Although body temperature fell in all pups after removal from the nest at 5 and 10 days of age, alcohol-exposed offspring consistently had lower temperatures during the test period and were slower to move to and huddle against a wall as a means of conserving body warmth in comparison to control pups. The difference in body temperature was no longer evident at 20 days of age, suggesting that prenatal alcohol exposure produced a developmental delay in thermoregulation. In addition, after being placed on the cool end of a thermal gradient, the alcohol-exposed pups moved farther toward the warm side than controls, suggesting that alcohol-exposed pups compensated behaviorally for the greater heat loss they experienced. Taken together, these data indicate that prenatal alcohol exposure impairs the ability of rat neonates to defend their body temperature and hence may underlie the altered thermal response to drug challenges observed in these animals later in adulthood (Abel et al. 1981; Nelson et al. 1986; Taylor et al. 1981, 1987).

Long-Term Behavioral Effects

One of the advantages of using laboratory animals in prenatal alcohol research is that the long-term effects of such treatment can be studied in a relatively shorter period of time than would be possible in humans. For example, Abel et al. (1987) reported on longevity associated with prenatal alcohol exposure in rats. These researchers found that in utero alcohol exposure significantly shortened the life span of laboratory rats by as much as 20 weeks (the approximate equivalent of one-seventh of a laboratory rat's life).

As outlined so far in this chapter, prenatal alcohol exposure has been shown to have adverse effects on a variety of neonatal behaviors that are vital for normal growth and development in animals and humans. These include motor dysfunctions, impaired feeding, and learning disabilities. In fact, prenatal alcohol exposure has been shown to produce deficits in associative learning in rats as early as 3 days of age (Barron et al. 1988). Many of the behavioral teratogenic effects of alcohol have been reported to be transient. That is, the effects appear to diminish with age, suggesting that prenatal alcohol exposure produces a developmental delay in CNS maturation (Abel 1982). Of course, some of this "normalization" of function may be due to the development of independent compensatory strategies designed to cope with and overcome the disabilities. Whether the recruitment of such compensatory mechanisms compromises the ability to perform other more complex functions later in life is not clear at present.

Nevertheless, animal research has revealed that some of the behavioral dysfunctions observed in young offspring are permanent, persisting into adulthood. For example, under particular testing conditions, behavioral abnormalities such as hyperactivity, tendency toward perseveration, and impaired performance in learning tasks have been observed in adult animals that were prenatally exposed to alcohol (Abel 1979; Abel and Dintcheff 1986a; Middaugh and Ayers 1988; Plonsky and Riley 1983; Randall et al. 1986). That some of these effects have been recently noted in rats more than a year old (Abel and Dintcheff 1986a,b) further attests to the permanence of these functional deficits. These findings also complement those of clinical studies that have revealed persistent attentional deficits in children of alcoholic mothers (Aronson et al. 1985; Spohr and Steinhausen 1987; Streissguth et al. 1984, 1986). Taken together, both basic and clinical studies have clearly established the long-lasting detrimental consequences of prenatal alcohol exposure. Studies aimed at distinguishing between those deleterious effects of in utero alcohol exposure that wane with maturity from those that are enduring are of particular clinical relevance, because the information gained from such studies would undoubtedly be important for targeting treatment and therapy for the affected children.

Effects on Stress Responsiveness

When placed in a stressful or dangerous situation, animals and humans respond similarly with the so-called "fight or flight" reaction. That is, the situation is either confronted (fight) or avoided (flight). In either case, myriad physiological and behavioral events are set in motion to ready the body for its response. One physiological component of the stress response is the stimulation of brain structures (hypothalamus and pituitary) that in turn activate the adrenal cortex to release corticosteroid hormones. Thus activation of the hypothalamic-pituitary-adrenocortical (HPA) axis, as measured by elevated levels of plasma corticosteroids, serves as a good index for assessing the ability of animals (including humans) to cope with a stressful event. In a recent series of studies, animal models were employed to examine the influence of prenatal alcohol exposure on the development of the HPA axis in offspring and to examine the activity of prenatal alcohol exposure under nonstressful and stressful conditions.

In one study, the effects of alcohol consumption on maternal HPA activity during pregnancy were assessed in a group of pregnant rats that consumed 36 percent of their total calories during pregnancy as alcohol, a second group that received the identical number of calories but with sucrose substituted for the alcohol-derived calories, and a third group that were maintained on standard chow and water (Weinberg and Bezio 1987). Alcohol consumption significantly increased maternal HPA activity, as indicated by elevated basal and stress-induced levels of plasma corticosteroids. It is important that this adrenocortical hyperactivity was shown not to be related to the nutritional status of the mothers, because neither suboptimal nor supraoptimal amounts of protein in the diets influenced the results. It is also significant that alcohol consumption during pregnancy was found to elevate maternal plasma corticosteroid levels during a period of time (gestation days 11-21) that corresponds with critical stages in the development of the fetal HPA axis. Thus the fetal HPA system may be altered as a function of maternal alcohol consumption because (a) alcohol can readily cross the placenta and directly activate the fetal HPA axis (which is functional before birth) and (b) elevated maternal corticosteroids (which also cross the placenta) may suppress fetal HPA activity. The investigators postulated that through some balance between these interacting prenatal influences, the fetal HPA axis may be perturbed as a result of maternal alcohol consumption (Weinberg and Bezio 1987).

Indeed, several studies have demonstrated that prenatal alcohol exposure influences the HPA axis in offspring after birth and later in adulthood. For example, it has been shown that plasma, brain, and adrenal corticosteroid levels are significantly higher in rats prenatally exposed to alcohol in comparison to controls at birth (Kakihana et al. 1980; Taylor, Branch, Cooley-Mathews, and Poland 1982; Weinberg 1989). During the first week of life, alcohol-exposed pups exhibited a blunted response to several stressors; the stress response was somewhat normal by the second week of life (Taylor et al. 1986; Weinberg 1989). However, this perturbation in basal and stress-related HPA activity early in life also has been shown to have long-term consequences on the manner in which these animals respond to stress in adulthood.

Although basal plasma corticosteroid levels are normal in adult rats prenatally exposed to alcohol, several studies have demonstrated that these animals exhibit a heightened stress response (elevated plasma corticosteroid levels) in comparison to control offspring. This augmented physiological response in adult rats prenatally exposed to alcohol was observed after exposure to a variety of sensory and emotional stimuli or situations, including noise, shaking, electric footshock, physical restraint, and being placed in a novel environment (Nelson et al. 1986; Taylor et al. 1981; Taylor, Branch, Liu, and Kokka 1982; Weinberg 1988). Similar results have been obtained after challenges with drugs such as ethanol and morphine (Nelson et al. 1986; Taylor et al. 1981). Moreover, recovery from the stress response was found to be retarded in offspring prenatally exposed to alcohol, and these animals were also shown to be less sensitive to manipulations that typically dampen the stress response (Weinberg 1988; Weinberg and Gallo 1982). It is interesting that the stress response to environmental or metabolic stressors, such as being exposed to a cold environment or fasting, did not differ between alcohol and control offspring (Taylor, Branch, Liu, and Kokka 1982). It appears that hyperresponsiveness to stress in prenatal alcohol-exposed offspring depends on the nature of the stressor itself.

The mechanism or mechanisms whereby alcohol exposure during fetal life heightens the HPA response to certain stressors later in adulthood are not clear at present. Some preliminary data have suggested that the effect may be centrally mediated because adrenal sensitivity to adrenocorticotropic hormone (ACTH), which is released by the pituitary and stimulates the production and secretion of corticosteroids from the adrenal cortex, is not altered as a function of prenatal alcohol exposure (Taylor, Branch, Lin, and Kokka 1982). On the other hand, elevated plasma ACTH levels were noted concomitant with higher plasma corticosteroid levels in rats prenatally exposed to alcohol following footshock stress (Nelson et al. 1986). Clearly, additional research will be needed to identify more specifically whether the pituitary and/or higher brain structures are altered in this capacity as a function of in utero alcohol exposure.

In addition to the enhanced hormonal (corticosteroid) response to stress, adult rats prenatally exposed to alcohol also demonstrate an augmented behavioral response to stress (Hannigan et al. 1987; Nelson et al. 1985). For example, after exposure to intermittent footshock, alcohol-exposed offspring displayed greater analgesia (reduced pain sensitivity) than controls (Nelson et al. 1985). This type of stress-induced analgesia can be blocked by administering a narcotic antagonist (naloxone), indicating that the analgesia is mediated by an endogenous opioid mechanism. In contrast, when an equivalent amount of footshock is presented continuously rather than intermittently, the resultant analgesia cannot be blocked by opiate antagonists. This type of stress-induced analgesia is apparently mediated by nonopioid mechanisms. The nonopioid form of stress-induced analgesia (that which follows continuous shock treatment) is not altered by prenatal alcohol exposure. Whether this distinction is related to alterations in brain opioid systems as a function of in utero alcohol exposure remains to be determined.

In summary, this line of research has demonstrated that prenatal alcohol exposure alters the development and activity of the HPA system early in life. In addition, fetal exposure to alcohol has long-term effects, altering both physiological and behavioral responsiveness to stress in adulthood. These perturbations may be of great significance with regard to offspring prenatally exposed to alcohol, because the ability to respond to and cope with a constantly changing and challenging (stressful) environment is crucial for survival and maintenance of normal life in animals and humans. Alterations in the HPA system may represent a contributing etiologic factor in the behavioral teratogenic actions of alcohol as well.

Effects on the Immune System

Children with FAS have been noted to be more susceptible to bacterial infections, which may be related to an immune deficiency characterized by depressed mitogenesis and dysgammaglobulinemia (Johnson et al. 1981). Animal research has recently begun to address how prenatal alcohol exposure may influence the development and functioning of the immune system. In one study, near-term mouse fetuses exposed to alcohol in utero were found to have reduced numbers of thymocytes and a diminished response to substances that ordinarily stimulate the immune system (Ewald and Frost 1987). Thymocytes are cells in the thymus that play an important role in the body's defense against infection.

In addition, rats at 21 days of age that were prenatally exposed to alcohol exhibited a diminished immunological response (T-lymphocyte proliferation) following a mitogen challenge (concanavalin A) in comparison to control offspring (Redei et al. 1989). The proliferative (immunological) response was eightfold lower in spleen and twofold lower in thymus cells from alcohol-exposed rats compared to responses measured in controls. This blunted immunological response also has been observed in adult rats prenatally exposed to alcohol (Norman et al. 1989). More specifically, the alcohol-exposed rats demonstrated a diminished proliferative response of concanavalin A-stimulated lymphoblast cells following interleukin-2 administration. These latter findings indicate that in utero alcohol exposure can have long-term effects on immune responsiveness. The investigators further postulated that, pending additional research, this biological response may be potentially useful as a marker for identifying individuals exposed to alcohol in utero.

Neuroanatomical and Neurochemical Effects

Another major advantage of using animals in fetal alcohol research is that it allows for the identification of structural CNS defects that may underlie observed functional (behavioral) deficits. Indeed, a number of neuroanatomical aberrations have been identified in animals prenatally exposed to alcohol (West and Pierce 1986), many of which also have been noted in clinical neuropathology studies (Clarren 1986). As more sophisticated experimental techniques have become available, these effects of prenatal alcohol exposure have been studied in more specific systems and with greater resolution.

The generation, proliferation, and migration of cerebral cortical neurons have been examined in rats who were exposed to alcohol in utero (Miller 1986, 1987, 1988). The investigator found that prenatal alcohol exposure delayed and extended the period during which neurons of the cerebral motor cortex were generated. Moreover, in comparison to control offspring, the mature cortex of prenatal alcohol-exposed rats contained fewer neurons and the distribution of these neurons was apparently altered. Normally, the organization of cortical neurons conforms to an inside-to-outside pattern of distribution. That is, neurons generated early in development reside in the deeper layers of the cortex, whereas those generated later are located in the superficial laminae. Prenatal alcohol exposure markedly altered this pattern of distribution; many late-generated neurons were found in the deeper layers of the motor cortex (Miller 1986, 1988).

Miller (1987) also studied the effects of prenatal alcohol exposure on the distribution and time of origin of cortical neurons that project to the spinal cord. During the course of normal development, the axons of these corticospinal neurons are pruned and their distribution in the cortex is restricted. However, adult rats who were exposed to alcohol in utero were found to have a greater number of these neurons, suggesting that the normal process of paring down corticospinal projections was altered. Miller suggested that because there was a delay in the origin of these neurons as well, these late-generated corticospinal cells may have been shielded from the normal pruning process. Whether the abnormal generation and migration of cortical neurons in animals prenatally exposed to alcohol results from aberrant glial processes that typically guide neuronal migration, the withdrawal of growth factors, and/or a disruption in neuron-neuron interactions that are critical for proper migration and orientation will require further investigation.

Other studies have demonstrated that acute alcohol exposure during critical periods of brain development can also have detrimental effects on the CNS. For example, administering a high dose of alcohol (5.8 grams per kilogram of body weight) to mice on a single day during the early phases of brain development (gestation day 7) resulted in gross brain malformations (Sulik et al. 1981, 1984). In another study with rats, oral administration of a total dose of 18 grams of alcohol per kilogram of body weight on gestation days 14 and 15 resulted in a thinner and severely disorganized cerebral cortex (Kotkoskie and Norton 1988). Days 14 and 15 are a critical period for the development of the cerebral cortex in rats. Finally, hippocampal mossy fiber development was found to be most vulnerable to alcohol insult during postnatal days 4 to 10 (West and Hamre 1985). Thus, both acute and chronic consumption of high doses of alcohol during pregnancy has been associated with aberrant CNS development in the rat offspring.

In addition to the pattern of alcohol exposure, brain regions have been shown to be differentially sensitive to alcohol-induced damage. As mentioned above, not all hippocampal cells are uni- formly affected by alcohol exposure (Dewey and West 1985a,b). In a more recent study, Pierce and West (1987) found that alcohol administered to rat pups on days 4 to 10 (corresponding to the brain growth-spurt period) caused a 31-percent reduction in brain weight compared to control animals that did not receive alcohol. However, the degree of growth retardation varied among different brain regions. Whereas the hippocampus was reduced by 26 percent in comparison to controls, the size of the dentate gyrus, a related hippocampal structure, was reduced by only 6.8 percent. Furthermore, within the hippocampus, certain substructures (sublaminae) were reduced in size by as much as 40.5 percent. Similarly, alcohol treatment reduced the tissue in the middle of the cerebellum by 14.5 percent, with the extent of the deficit varying in different cerebellar substructures. The implication of these findings is that different regions of the developing brain may have different thresholds and perhaps different critical periods of susceptibility to alcohol injury. This implication further complicates the question of how much alcohol exposure is harmful to the developing brain. The answer may be that it depends not only on the pattern and timing of the alcohol exposure but on the brain region as well (West 1987).

The level of analysis for neurochemical investigations has also become more sophisticated. Whereas many of the earlier studies examined neurotransmitter levels in whole brain tissue, more recent work has focused on steady-state levels as well as utilization and receptor function of transmitter systems in more specific brain regions. The monoamine neurotransmitters, particularly serotonin, have been studied in greatest detail. The cerebral cortices of rats prenatally exposed to alcohol throughout pregnancy were found to be deficient in serotonin and its major metabolite (5-HIAA) by as much as 50 percent in comparison to controls (Rathbun and Druse 1985). Decreased levels of serotonin were also detected in the cerebellum and brainstem, but not in other brain regions, including the hippocampus, hypothalamus, and striatum. This indicates that prenatal alcohol exposure has localized effects on neurotransmitter systems.

More recently, prenatal alcohol exposure was shown to alter serotonin uptake processes in the motor, but not somatosensory, cortex of 19- and 35-day-old rats (Druse and Paul 1988). In addition, in utero alcohol exposure was shown to alter specific serotonin receptor subtypes. More specifically, rats prenatally exposed to alcohol evidenced a decreased number of serotonin subtype 1 receptors in both motor and somatosensory cortices (Tajuddin and Druse 1988a). In contrast, prenatal alcohol exposure did not significantly influence the number of serotonin subtype 2 receptors (Tajuddin and Druse 1988b). These effects on the serotonin system are particularly interesting because serotonin not only is implicated in mediating a variety of neurobehavioral functions but also is thought to play an important role in neuronal maturation and differentiation during embryonic development (Lauder et al. 1983).

In addition, there is some recent evidence to suggest that these reported neuroanatomical and neurochemical aberrations may result in, or be related to, an alteration in brain activity (Miller and Dow-Edwards 1988; Vingan et al. 1986). These studies employed an autoradiographic 2-[14C]deoxyglucose technique to examine the rate of glucose use in several brain regions of adult prenatally alcohol-exposed and control offspring. This in vivo method allows for the measurement of glucose incorporation in localized brain regions, which is directly related to functional activity (Sokoloff 1981). Prenatal alcohol exposure was found to decrease glucose use significantly in sensory and motor cortex regions as well as in numerous limbic system structures including the hippocampus (Miller and Dow-Edwards 1988; Vingan et al. 1986). Thus, as demonstrated in neuroanatomical and neurochemical studies, the effect of prenatal alcohol exposure on the metabolic activity of the brain is localized to specific brain regions as well.

In summary, animal research has revealed that prenatal alcohol exposure both alters the cytoarchitectural structure and metabolic activity of numerous brain regions and perturbs a variety of neurotransmitter systems. These effects have been identified in animals that exhibit no external physical abnormalities and thus may represent the neurobiological substrates for the behavioral teratogenic actions of alcohol. This contention is further supported by the fact that many of the affected brain regions and neurotransmitter systems have been implicated in mediating behavioral functions that are also particularly susceptible to prenatal alcohol exposure, such as sensorimotor dysfunctions and learning disabilities. Although some studies have been designed to examine the brains of animals that exhibited these functional deficits (Abel et al. 1984; Vingan et al. 1986), additional studies of this nature are needed. In addition, the recruitment of other more sophisticated neurobiological techniques, such as nuclear magnetic resonance (NMR) brain imaging procedures, will provide further insight into the relationship between structural and functional deficits that result from prenatal alcohol exposure.

Alcohol Teratogenesis in a Nonhuman Primate Model

Although rodent models have been most commonly employed to study prenatal alcohol effects in the laboratory, there are clear limitations to extrapolating findings from mice and rats to humans. For example, because rodents have a much faster metabolic rate than humans, they typically require very high alcohol doses to produce measurable blood alcohol levels and FAE. Therefore the potential effects of low or moderate drinking on pregnancy outcome in humans are difficult to model using rats or mice. In addition, the period of greatest brain growth and development, which occurs in late gestation in humans, primarily occurs postnatally in rodents. Thus, in order to correspond to the human third-trimester equivalent, alcohol needs to be delivered to rodent offspring postnatally, rather than in utero. Although sophisticated techniques have been developed for the postnatal delivery of alcohol to artificially reared pups (Diaz and Samson 1980; West et al. 1984), maternal variables are necessarily eliminated from the procedure. Hence, nonhuman primate models would be useful in clarifying the relationship between alcohol-related birth defects and the dosing and timing parameters relevant to human pregnancy. Finally, approximating the neurobehavioral effects of prenatal alcohol exposure observed in humans is difficult in rodents because of their limited cognitive capacity. For these reasons, primate models of FAS have been developed.

Clarren and his colleagues have been studying the effects of intermittent alcohol administration to pregnant Macaque monkeys. Fifty-four pregnant monkeys were included in a recent study in which alcohol was given orally in varying doses (0.3 to 4.1 grams per kilogram of body weight) once per week so that the peak plasma ethanol concentration (PPEC) ranged between 24 and 549 milligrams per deciliter. This pattern of exposure was designed to model binge drinking in humans. A control group of monkeys received a sucrose solution isocaloric to the highest dose of alcohol. Of the initial 54 pregnant monkeys, 33 gave birth to live infants. The rate of spontaneous abortion significantly increased at the alcohol dose of 1.8 grams per kilogram of body weight. This abortifacient effect occurred at PPEC of 205 milligrams per kilogram and higher (Clarren, Bowden, and Astley 1987). At 6 months of age, the 33 infants were examined. Although no animal showed all the features of the human FAS, facial anomalies, growth deficiencies, and CNS dysfunction were found in 57 percent (16 of 28) of the alcohol-exposed monkeys. Moreover, these alcohol-related birth defects greatly resembled those documented in children with complete or incomplete features of FAS. None of the control monkeys exhibited these abnormalities (Clarren et al. 1988). Studies examining the neuroanatomical and neurochemical profiles of these animals are currently under way and will undoubtedly provide important information with regard to structure-function relationships.

Studies on Mechanisms of Fetal Alcohol Damage

The study of mechanisms underlying alcohol teratogenesis holds some promise for devising effective preventive and/or intervention measures for FAS and FAE. As with any other disease state, understanding the underlying mechanisms of FAS is essential for developing such treatment strategies. Although the pathophysiology of FAS remains undetermined, studies on the mechanisms of alcohol-induced fetal damage have increased in recent years. This work has focused primarily on five general areas: placental dysfunction, nutritional deficiency, acetaldehyde (ACH) toxicity, fetal hypoxia (impaired delivery of oxygen to the fetus), and the role of prostaglandins.

Maternal alcohol consumption has been shown to impair uptake and transport of essential amino acids by placentas derived from rodents, monkeys, and humans (Fisher et al. 1981, 1983; Henderson et al. 1982; Lin 1981). This alteration in placental functioning, however, was not found after brief exposure to alcohol (Schenker et al. 1989). Nevertheless, placental dysfunction may play a role in the pathophysiology of FAS. However, it does not appear to constitute the sole underlying mechanism, because alcohol has been demonstrated to have a detrimental effect on growth and development in a chick model (Pennington et al. 1983) and in rat embryos incubated in culture (Brown et al. 1979; Priscott 1982), two model systems in which the placenta plays no role in embryonic development.

Another potential factor in FAS is nutritional deficiency arising from maternal alcoholism. Nutritional and mineral deficiency is known to accompany chronic alcohol exposure. However, its role in FAS remains unsettled since protein supplementation has been found in some cases to ameliorate the adverse effects of alcohol (Wiener et al. 1981) but in others failed to improve pregnancy outcome (Weinberg 1985).

The role of ACH (the primary metabolite of alcohol) in the pathogenesis of FAS has also not been resolved. In some studies ACH administration was found to be teratogenic (O'Shea and Kaufman 1979; Dreosti et al. 1981), whereas others have reported negative findings (Blakely and Scott 1984; Webster et al. 1983). Discrepant results also have been reported in studies in which ACH was applied to the medium of rat embryos grown in culture (Campbell and Fantel 1983; Priscott 1985). In addition, it is not clear whether ACH reaches the fetus by placental production or solely by transfer from maternal circulation. Recently, a study was conducted to address this issue in human placental tissue. With a human placental perfusion system, it was shown that the placenta has the capability to metabolize alcohol, as measured by the presence of ACH in the fetal perfusate. In addition, when ACH was administered to the maternal side of the placenta, it was transferred to the fetal side, reaching approximately 50 percent of the maternal concentration (Karl et al. 1988). The authors suggested that the human placenta may play a pivotal role in the pathophysiology of alcohol-associated fetal damage. However, given the negative results in studies cited previously in this chapter, it appears that ACH is a contributor to, rather than a cause of, FAS and FAE.

Fetal hypoxia also has been implicated in the pathophysiology of FAS. Support for this notion comes from a study in which maternal alcohol exposure was found to impair umbilical circulation in monkeys. Intravenous administration of 3 grams of alcohol per kilogram of body weight, which resulted in a peak blood alcohol level of 250 milligrams per deciliter, produced a collapse of the umbilical vessels within 10 to 15 minutes after injection. Analysis of blood gases revealed that this effect, albeit transient, was sufficient to produce a severe oxygen-deficient state for the fetus (Mukherjee and Hodgen 1982). More recent studies with human umbilical cords have demonstrated similar effects following in vitro alcohol administration (Altura et al. 1983; Yang et al. 1986; Savoy-Moore et al. 1989). Although decreased fetal-placental blood flow has been shown to be associated with intrauterine growth retardation (Fleischer et al. 1985), a cardinal feature of FAS, it remains to be determined whether fetal hypoxia results in structural birth defects similar to those reported following prenatal alcohol exposure.

Finally, prostaglandins (potent hormonelike compounds) have been implicated in the pathogenesis of FAS. Pharmacologic agents such as aspirin, which inhibit the synthesis of prostaglandins (Vane 1978), have been shown to reduce the incidence of alcohol-induced birth defects (Randall and Anton 1984; Randall et al. 1987b) and attenuate alcohol-induced growth retardation in an animal model (Pennington et al. 1983). These data suggest that alcohol's teratogenic actions may be mediated by an increase in prostaglandin levels (Randall et al. 1987a). However, future studies will need to measure directly prostaglandin levels to verify such a relationship. It also should be noted that because some prostaglandins alter blood pressure, an imbalance in the prostaglandin system may result in reduced umbilical blood flow and hence in impaired oxygen and nutrient supply to the fetus.

In summary, with the teratogenic actions of alcohol firmly established, more recent attention has been focused on the underlying mechanisms. To date, results from basic research have advanced several possibilities, including impaired placental transfer of essential nutrients, ACH toxicity, fetal hypoxia, and perturbation of prostaglandins. All of these potential mechanisms probably represent etiologic factors and in combination may collectively play a role in alcohol-induced teratogenesis. It therefore is quite possible that more than one mechanism is involved in FAS, and that different features of FAS may be the manifestation of different pathophysiologies.

Public Awareness and Policy

Since FAS was identified, educational and public service efforts have been mounted that have contributed to an increased public awareness of the dangers associated with drinking while pregnant. This increase in awareness is borne out by results from the 1985 National Health Interview Survey. As part of the Health Promotion and Disease Prevention Questionnaire, about 20,000 men and women aged 18 to 44 answered questions about their awareness of the risks of smoking and drinking during pregnancy. Approximately 84 percent of the respondents associated heavy drinking with increased risk for adverse pregnancy outcomes (Fox et al. 1987). In fact, smoking was perceived to be a lesser risk than heavy drinking. However, a much smaller proportion were knowledgeable about FAS. Among the 55 percent who had heard of FAS, only one in four correctly identified the syndrome as a set of birth defects. Seventy percent identified the syndrome as representing alcohol addiction in the newborn (Williams et al. 1986). Similar results have been obtained in a public attitude and awareness survey conducted in Australia (Oei et al. 1986). These findings suggest that although many people are aware of increased risks associated with heavy drinking during pregnancy, there is a need to educate young adults on the specific harmful effects of alcohol exposure on the developing fetus. Moreover, despite the reported increase in general awareness of an increased risk, FAS and FAE remain a major public health problem.

With regard to public policy, the 1981 surgeon general's advisory, which recommended abstinence during pregnancy, bolstered educational efforts (USDHHS 1981). In addition, effective in November 1989, it is unlawful to manufacture, import, or bottle any alcoholic beverage unless the container in which it is sold bears a warning about the risks of drinking while pregnant. Future research should assess whether this requirement has an impact on knowledge, attitudes, or behavior related to alcohol consumption during pregnancy.

Summary

The public education effort surrounding FAS since it was identified in 1973 has resulted in widespread public awareness of the syndrome: in a 1985 national survey, about 84 percent of respondents associated heavy drinking with increased risk of adverse pregnancy outcomes. At the same time, however, FAS and FAE are now costing nearly a third of a billion dollars a year to treat and are among the leading known causes of mental retardation in the Western world.

The diagnostic criteria for FAS comprise prenatal and postnatal growth retardation, a characteristic constellation of craniofacial anomalies, CNS dysfunction, and major organ system malformation. When only some of these criteria are met, the diagnosis is FAE. The harmful effects of prenatal exposure to alcohol are now known to exist on a continuum, ranging from gross morphological defects at the more severe extreme, to more subtle cognitive-behavioral dysfunctions at the other.

A followup study of FAS cases in Germany showed improvement on several levels, particularly with regard to physical appearance, but cognitive deficiencies persisted; the authors reported that many of the study population required special education. Furthermore, the study revealed persistence in the positive correlation between degree of mental disability and physical dysmorphology noted in children initially diagnosed with FAS.

Not all women who drink alcohol excessively during pregnancy deliver babies with FAS or even FAE. Genetic and maternal variables may explain why some infants are spared. For example, epidemiological studies have shown that black infants are at greater risk.

An ongoing longitudinal study being conducted in Seattle is showing that attentional deficits in children whose mothers drank heavily during pregnancy endure in children in their school-age years. Future studies will need to investigate how long these deficits persist and if they hamper classroom learning.

Questions of threshold doses and critical periods of exposure, although of great concern to scientists and the public, are slow to be answered because of the lack of a specific physiologic measure that accurately reflects alcohol consumption. Self-underreporting of alcohol consumption is a problem, and repeated blood sampling is infeasible. Because of this problem, animal models are particularly useful to researchers.

In using animal models, researchers are able to control for other variables such as malnutrition, poor rearing (environmental) conditions, disease, smoking, and other drug use. Studies with rodents, the most commonly used, have provided clues to the relationship between FAE and certain specific cellular, neurological, and hormonal irregularities.

With the teratogenic actions of alcohol firmly established, more recent attention has been focused on identifying the underlying mechanisms. To date, results from basic research have advanced several possibilities, including impaired placental transfer of essential nutrients, ACH toxicity, fetal hypoxia, and perturbation of prostaglandins. It is possible that more than one mechanism is involved in FAS, and that different features of FAS may be the manifestation of different pathophysiologies.

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Chapter VII

Adverse Social Consequences

Introduction

Adverse social consequences arise as a result of single episodes of drinking, persistent alcohol abuse, and alcohol dependence. These consequences can affect not only the drinker but also the drinker's family, friends, and associates, as well as others with whom the drinker may come in contact. Moreover, the cost to society of adverse outcomes of alcohol use is high. In addition to alcohol-involved motor vehicle crashes, alcohol use and abuse have been linked to other types of accidental injuries and fatalities, including drownings, falls, and burns. Alcohol may also increase the severity of trauma incurred in accidents. Individuals with alcohol-related problems require more general health care, may be less productive at their jobs than individuals who do not abuse alcohol, and are also overrepresented among criminals and suicides. The negative impact that these and other alcohol-related problems have on the quality of life of society is paralleled by considerable economic cost. It has been estimated that the cost to the United States in 1990 due to alcohol dependence and abuse will reach $136.3 billion (Harwood et al. 1985).

This chapter highlights recent research addressing the relationship between alcohol use and related adverse social consequences.

Accidents

Alcohol has been implicated in the four leading causes of accidental death in the United States—motor vehicle crashes, falls, drownings, and fires and burns.

Motor Vehicle Crashes

The National Highway Traffic Safety Administration (NHTSA) defines a fatality or traffic crash as alcohol involved or alcohol related when a participant (driver, pedestrian, or bicyclist) has a measured or estimated blood alcohol concentration (BAC) of 0.01 percent or above (NHTSA 1988c). NHTSA defines a collision in which one of the active participants was drunk (BAC of 0.10 percent or greater, the legal limit for intoxication in most jurisdictions) as a high-level alcohol crash (NHTSA 1988c). Recent research has examined high-level alcohol crashes as well as those in which participants had lower BAC levels.

Motor vehicle crashes are the leading cause of injury deaths in the United States (Baker et al. 1984). During 1987, 46,386 people in the United States died in traffic crashes. Approximately one-half of these fatalities were alcohol related (NHTSA 1988c). It has been estimated that the risk of a fatal crash, per mile driven, may be at least eight times higher for a drunk driver (BAC of 0.10 or greater) than for a sober one (Fell 1987).

In a recent U.S. national survey, 6.1 percent of adults responded positively when asked if they had driven "when you've had perhaps too much to drink" during the previous month (Bradstock et al. 1987). Among individuals in a Canadian survey who reported drinking during the previous month (Wilson and Jonah 1985), 35 percent reported driving after drinking on one or more occasions when they did not believe themselves to be impaired, and 13 percent reported driving on one or more occasions when they thought they may have been legally impaired. When drivers were stopped and given a roadside breath analysis in a nationwide U.S. study (Wolfe 1986), about 3 percent had BACs higher than 0.10 percent; approximately 80 percent had BACs of less than 0.02 percent.

The Fatal Accident Reporting System (FARS) of NHTSA contains data on all fatal traffic crashes in all States and includes BAC levels whenever available. In the past 7 years, the BAC reporting rate has increased from 25 to 71 percent for fatally injured drivers and from almost 0 to 22 percent for surviving drivers (NHTSA 1988a). FARS data indicate that the proportion of drivers killed in traffic accidents who had BACs equal to or greater than 0.10 percent decreased from 46 percent in 1980 to approximately 38 percent in 1987. The proportion of all people killed in crashes in which at least one participant had a BAC of 0.10 percent or greater declined from 46 percent in 1982 to 40 percent in 1987 (NHTSA 1988c).

Nonetheless, traffic crashes remain the greatest single cause of death in the United States for people between the ages of 5 and 34 (NHTSA 1988c). Estimates based on FARS data combined with vital statistics data indicated that, in 1986, motor vehicle injuries were the predominant cause of years of potential life lost (YPLL) by individuals under the age of 65 (USDHHS 1988) and accounted for 11.9 percent of total YPLL in the United States (see fig. 1). YPLL is calculated by subtracting the actual age at death from 65. More than half of the total YPLL lost as a result of motor vehicle injuries were due to alcohol-related injuries, which accounted for 6.8 percent of the total YPLL. Crashes involving intoxicated drivers (BACs greater than or equal to 0.10 percent) were responsible for 44.5 percent of all YPLL due to motor vehicle injuries and for 5.3 percent of the total YPLL.

About 40 percent of all teenage deaths (ages 15 to 19) occur in traffic crashes (NHTSA 1988c). However, the number of fatal teenage crashes involving drunk drivers decreased from 2,187 in 1982 to 1,494 in 1987, while the total number of fatal crashes for this age group increased from 7,690 to 8,052. These data indicate that although more young drivers are becoming involved in fatal crashes, fewer of them are intoxicated at the time of the crash (NHTSA 1988c).

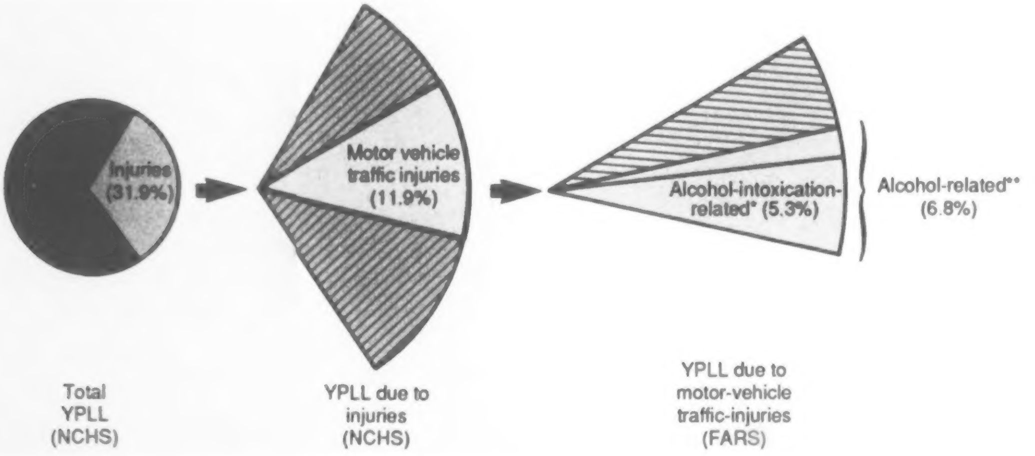

FIGURE 1. Contribution of alcohol-related and alcohol-intoxication-related motor vehicle traffic injuries to total years of potential life lost (YPLL) before age 65, United States, 1986.

*Drivers' BACs were greater than or equal to 0.10 percent.

**Drivers' BACs were greater than or equal to 0.01 percent.

SOURCE: Modified from USDHHS 1988.

Alcohol involvement occurs more frequently in fatal crashes at night than during the day, and more frequently on weekends than on weekdays. According to FARS data on fatal accidents from 1982 to 1986, the greatest reduction in the involvement of drivers with BAC levels of 0.10 percent or more took place during the daytime hours, both on weekdays and on weekends, among drivers aged 16 to 20 and over 45 years, and among female drivers (NHTSA 1988a). During this period, alcohol involvement in fatal accidents decreased for drivers of heavy trucks, passenger cars, light trucks and vans, and medium trucks but increased slightly for drivers of motorcycles (NHTSA 1988a) (see table 1). In motor vehicle crashes during 1986 that involved a pedestrian or a bicyclist and an automobile driver, more pedestrians and bicyclists were legally intoxicated (29.9 percent) than automobile drivers (17.7 percent).

The National Accident Sampling System (NASS) of NHTSA also collects data on alcohol-related injuries from motor vehicle accidents. NASS uses nationwide teams to investigate a random sample of police-reported traffic crashes (NHTSA 1988b). Although it has been estimated that there may be twice as many unreported crashes as reported crashes, the majority of the unreported crashes involve only minor property damage and no significant personal injury (NHTSA 1988b).

In a NASS report on police-reported crashes in 1986, 9 percent involved alcohol. In other words, a participant in the crash had a BAC of at least 0.01 percent, a driver was cited for driving while intoxicated (DWI), or a police statement alleged alcohol involvement. However, because most cases were based on police judgment alone, NASS data probably understate the alcohol involvement (NHTSA 1988b).

Of the alcohol-involved crashes in the NASS investigation, almost 50 percent resulted in minor to moderate injuries; 37 percent of non-alcohol-involved crashes resulted in this degree of injury. Eight percent of the alcohol-involved crashes resulted in serious to maximum injuries compared with 2 percent of the non-alcohol-involved crashes (NHTSA 1988b).

Figure 2 shows alcohol involvement in reported crashes by license status. Drivers in reported crashes with suspended, revoked, or no licenses were five times likelier to have been drinking, and drivers with expired licenses were almost three times likelier to have been drinking, as drivers with valid licenses. Drivers not using seat belts were more than three times likelier to have been drinking as drivers using seat belts (NHTSA 1988b).

In summary, while the proportion of intoxicated persons (drivers, pedestrians, or bicyclists) killed in fatal crashes has been declining, approximately one-half of all crash fatalities have been alcohol related. Further, traffic crashes continue to be the single leading cause of death for people between the ages of 5 and 34. To address this problem, a variety of preventive educational and policy measures have been implemented, with varying degrees of success (see chapter IX for a discussion of research evaluating these approaches). Intervention strategies, also varying in effectiveness, have been targeted at DWI offenders to reduce both drinking problems and driving after drinking (research on interventions for DWI offenders is discussed in chapter X).

Accidental Drownings, Falls, and Fires and Burns

Although less is known about the contribution of alcohol to drownings, falls, and fires and burns

TABLE 1. Reduction in involvement of drivers with BACs of 0.10 percent or higher in fatal crashes by vehicle type, 1982 versus 1986

	Percent		
Vehicle type	**1982**	**1986**	**Reduction**
Motorcycles	40.7	41.0	-1
Passenger cars	36.7	27.5	25
Light trucks and vans	36.3	30.9	15
Medium trucks	7.2	6.2	14
Heavy trucks	4.2	2.6	38

SOURCE: NHTSA 1988a.

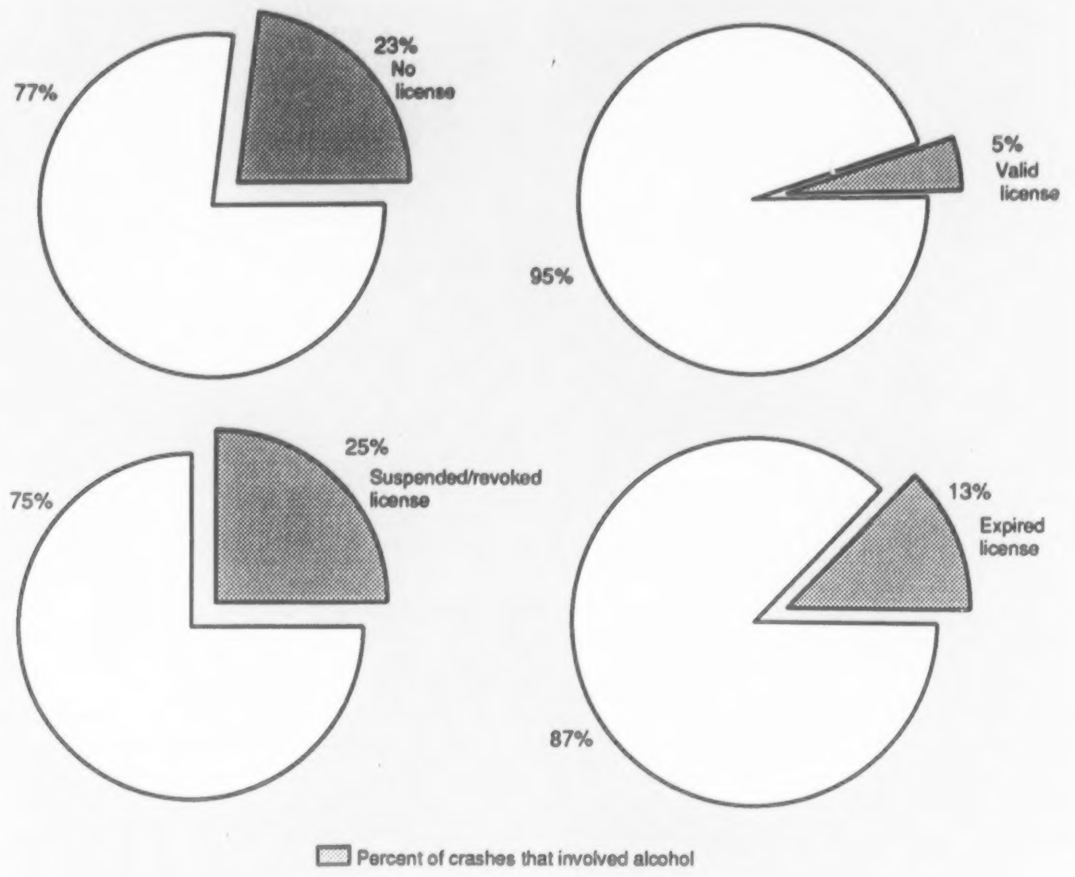

FIGURE 2. Alcohol-involved crashes as a function of license status, 1986.
SOURCE: Adapted from NHTSA 1988b.

than about its contribution to vehicular accidents (Howland and Hingson 1988b), findings of a recent study that reviewed 4 years of medical examiner records in a New Jersey county indicated that a history of alcohol problems or alcohol consumption immediately before a fatal accident occurred more often in deaths by falls and fires than in traffic deaths (Haberman 1987). Research suggests that alcohol increases the risk for falls, fires, and burns, but evidence of alcohol's relationship to drowning is, at present, inconclusive (Howland and Hingson 1988b).

Falls

Falls are the most common cause of nonfatal injuries in the United States and the second leading cause of fatal accidents, accounting for approximately 13,000 deaths a year (Baker et al. 1984). Hingson and Howland (1987) reviewed 21 studies published from 1950 to 1985 on alcohol and falls. The data generally suggest that alcohol increases risks for falls. In these studies, the percentage of alcohol-related fatal falls ranged from 17 to 53 percent and the percentage of alcohol-related nonfatal falls ranged from 21 to 77 percent. Although most of the study designs did not allow a determination of causality, the inclusion of a control group in one study conducted in Finland (Honkanen et al. 1983) permits the inference that alcohol increases risks for falls.

Honkanen et al. (1983) reported that of 313 emergency room patients who had suffered accidental falls, 60 percent had measurable BACs and 53 percent had BACs above 0.2 percent. These patients were compared to control subjects—pedestrians who were at the accident site 1 week later and at the same time of day as the accident patients. The control subjects were measured for BAC and they were also matched in sex and age to patients. Comparison of the two groups allowed the relative risk of falls for different BAC levels to be estimated. The risk of falls for individuals with BACs of 0.05 to 0.10 percent was found to be 3 times greater than that for individuals with no exposure to alcohol, 10 times greater for individuals with BACs of 0.10 to 0.15 percent, and about 60 times greater for individuals with BACs of 0.16 percent or higher.

Fires and Burns

Fires and burns are the fourth leading cause of accidental deaths from injuries in the United States and are responsible for an estimated 6,000 fatalities a year (Baker et al. 1984). Howland and Hingson (1987) analyzed 32 studies published between 1947 and 1986 on alcohol and injuries from fires and burns. As in research dealing with drowning and falls, these studies were primarily descriptive and did not include control populations that had not received burns. However, a number of the studies provide suggestive evidence associating alcohol consumption with increased risk of fires and burns.

Some of the evidence on increased risk of fires and burns associated with alcohol consumption comes from studies of treated alcoholics. A study of alcoholics in treatment in Toronto between 1951 and 1963 found that the rate of death by fire was 9.7 times the rate expected on the basis of Ontario mortality statistics (Schmidt and de Lint 1972). The proportion of deaths by fire among treated alcoholics studied in St. Louis (Combs-Orme et al. 1983) was 26 times the expected rate based on St. Louis mortality data. Neither of these studies, however, reported whether subjects were drinking before the fatal fires.

Other evidence has been provided by research examining deaths in the general population. A study conducted in California (Waller 1972) on a series of nonvehicular deaths between 1965 and 1967 indicated that 64 percent of the individuals whose deaths were attributed to fire had BACs greater than or equal to 0.10 percent at the time of death. Of the individuals who died after episodes of acute illness, 18 percent had BACs greater than or equal to 0.10 percent at the time of death.

Ten of the studies reviewed by Howland and Hingson (1987) provided data about complete series of burn fatalities and compared fatal burn victims who had BACs equal to or greater than 0.10 percent with other burn victims. In these studies, the percentage of intoxicated burn victims ranged from 37 to 64 percent with a median value of 48 percent (Howland and Hingson 1987). Assuming that less than 48 percent of the general population is intoxicated at any given time, the authors interpreted these data as suggesting that alcohol exposure is a risk factor for fire deaths. A number of the studies reviewed also indicated that alcohol exposure was more frequent among victims of cigarette fires. This observation, combined with evidence that house fires involving cigarettes account for approximately one-third of all fire fatalities, suggests that alcohol use in combination with smoking presents a serious risk for fire and burn injuries (Howland and Hingson 1987).

Drownings

Drowning ranks as the third leading cause of accidental death in the United States (Baker et al. 1984). Research findings suggest that victims have been exposed to alcohol in approximately 38 percent of drowning deaths (Howland and Hingson 1988b).

A person under the influence of alcohol may be more susceptible to drowning because of disorientation, exacerbated thermal response to water temperature, impairment of psychomotor skills, and reduced ability for breath holding (National Transportation Safety Board 1983). To date, however, available research data do not allow firm conclusions to be drawn about a causal role for alcohol in drownings. Determining whether alcohol increases the risk for drowning requires comparing the BACs of all individuals in a given population at risk for drowning—e.g., all those at a particular beach, swimming pool, or waterway—with the BACs of drowning victims. To assess available evidence on the relationship of alcohol to risk of drowning, Howland and Hingson (1988a) reviewed 36 studies published between 1950 and 1985. For the most part, data from these studies could not be used to establish a causal relationship between alcohol and drowning because they were descriptive and did not compare BACs of drowning victims and other individuals engaged in activities on or near the water (Howland and Hingson 1988a).

A recent survey of boat owners, conducted by a boat owners' interest group (BOAT/US, cited in Howland and Hingson 1988a), indicated that 35 percent of the boaters drank while under way. This figure is comparable to the findings of a Coast Guard survey that 40 percent of 15 million boaters reported carrying alcohol on outings (Wright 1985). Studies reviewed by Howland and Hingson (1988a) that analyzed drownings during boating suggested that from 17 to 31 percent of the boaters who drown had consumed alcohol. Since the consumption of alcohol by boaters who drown is similar to and possibly less than the consumption by boaters in general, these data suggest that any causal association between alcohol and drowning in boating accidents may be weak (Howland and Hingson 1988a).

Assessing Alcohol's Role in Accidents

The need for improvement in the measurement of alcohol's role in accidents has been emphasized recently. Improved assessment would (1) supply data needed for planning and providing direct services, (2) provide a baseline for evaluating prevention and intervention programs, and (3) improve estimates of the economic costs of alcohol abuse (Grant et al. 1987).

The need for routine BAC testing in emergency rooms has been noted (Roizen 1988). Research indicates that most emergency rooms do not test routinely for alcohol in accident victims. A national survey of trauma centers (Soderstrom and Cowley 1987) found that although two-thirds of the centers estimated that the majority of their patients had consumed alcohol, only 55 percent routinely conducted BAC tests at patient admission. Reviews of emergency patient charts (Chang and Astrachan 1988) and a statewide survey of emergency room physicians (Simel and Feussner 1988) also revealed low use of BAC testing. A review of emergency room studies (Roizen 1988) indicated that, even when a concerted effort is made, up to one-third of patients admitted to emergency rooms are not tested. Development of a feasible means of measuring BAC at the scene of an accident could also reduce underreporting of alcohol involvement in accidents.

Another focus is the need to code acute alcohol involvement related to injuries. The diagnostic codes currently available in *International Classification of Diseases* (ICD) are appropriate for identifying chronic conditions related to alcohol but are not useful for indicating acute alcohol involvement at the time of an accident. The Alcohol, Drug Abuse, and Mental Health Administration of the U.S. Public Health Service has recently recommended the addition of two supplementary alcohol-involvement codes for ICD-10, the upcoming tenth revision of this coding system (Grant et al. 1987). The recommended codes identify alcohol involvement based on BAC and on level of intoxication.

Underuse of existing codes may also reduce the usefulness of measurement efforts. Towle et al. (1988) found that "E codes" (accident codes in the clinical modification of ICD-9 [ICD-9-CM] [Commission on Professional and Hospital Activities 1978]), which provide information on the circumstances surrounding injuries, were underused in hospital discharge reports. If this information is not provided consistently, discharge records cannot be useful for developing accurate estimates of alcohol involvement in various kinds of accidents.

Another problem affecting measurement is the wide variety of settings in which alcohol-related injuries are treated (Towle et al. 1988). Because of this variety, one surveillance system cannot capture all accidents and injuries (Towle et al. 1988), and combining data is difficult because the various agencies that collect information on alcohol-related problems use different coding schemes (Westermeyer 1988).

Comparisons of data on the temporal pattern of alcohol consumption with data on injury incidence have been suggested recently as a means of assessing the involvement of alcohol in accidents. Arfken (1988) found positive correlations between the temporal pattern of drinking based on data from a national household drinking survey and FARS and NASS data on motor vehicle accidents (see fig. 3) and has suggested that this approach could be used to analyze other injuries suspected to be alcohol related, such as pedestrian fatalities and drowning.

Suicide

Research indicates that 20 to 36 percent of suicide victims have a history of alcohol abuse or were drinking shortly before their suicides (Roizen 1982; Colliver and Malin 1986). Recent studies have reported findings indicating relationships between alcohol, suicide, and use of firearms (Hlady and Middaugh 1988; Brent et al. 1987; Welte et al. 1988).

It has been suggested that alcohol tends to be associated with suicides that are impulsive rather than premeditated (Welte at al. 1988). The results of a recent study of suicides in a New York county from 1972 to 1984 (Welte et al. 1988) showed that suicides with detectable BACs received lower scores when rated on a predictability scale that allotted points for the following factors: left a note, diagnosed as depressed, poor health, prior suicide attempt, under psychiatric

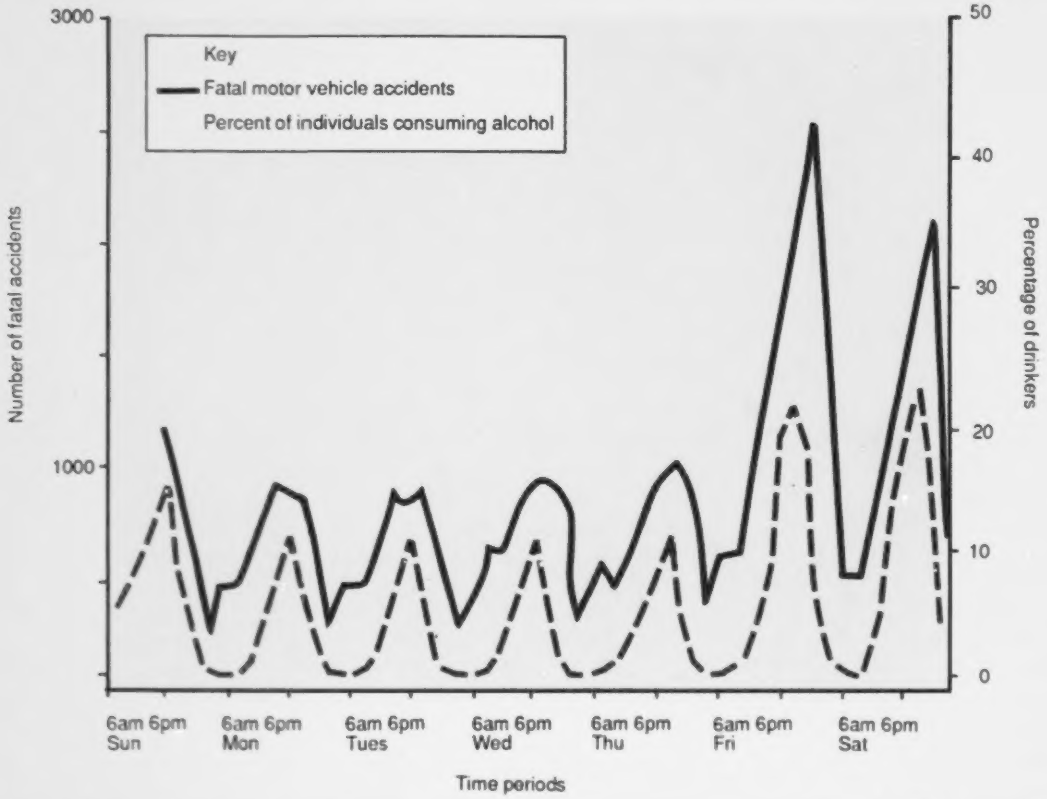

FIGURE 3. Temporal patterns of alcohol consumption and fatal motor vehicle accidents.
SOURCE: Arfken 1988. Copyright 1988 by the Research Society on Alcoholism.

care. They were also more likely to have died of gunshot wounds.

Youthful suicides also have shown a relationship between alcohol and use of firearms. A study conducted by Brent et al. (1987) found that the suicide rate among residents of a Pennsylvania county, aged 10 to 19, doubled from 1960 to 1983. Data were adjusted to control for improved ascertainment of suicide over the 24-year study period. Positive BACs were found in 12.9 percent of youthful suicides in 1968 to 1972, in 25.5 percent in 1973 to 1977, and in 46.0 percent in 1978 to 1983; there were no significant changes during this period in the proportion of young suicide victims under the influence of other drugs. The rate of suicide by firearms increased more rapidly than suicide by other means. Those victims with a detectable BAC at the time of death were almost 5 times likelier to use firearms as a means of suicide than victims with no detectable BAC; victims who were intoxicated (BAC equal to or greater than 0.10 percent) were almost 7.5 times likelier to use firearms. However, the findings of this study were inconclusive about the impulsivity or predictability of the youthful suicides: little variation occurred over the study period in proportion of indicators of suicidal intent (efforts to conceal attempts, suicide notes, evidence of preparation), symptoms of depression, and history of psychiatric treatment.

A study of suicides in Alaska also found an association between alcohol and suicide by gunshot wounds (Hlady and Middaugh 1988). During 1983 and 1984, 59 percent of suicides in Alaska had detectable BACs and 31 percent had BACs of greater than 0.10 percent. Alaska Natives, while only 14 percent of the State's population, accounted for 33 percent of the suicides during the period. Native suicides were more than twice as likely as white suicides to have BACs greater than 0.10 percent. Suicides with BACs greater than 0.10 percent were more likely than others to have died as a result of gunshot wounds.

Further research investigating different populations will be required to determine the nature of the relationship between use of firearms, alcohol, and suicide as well as the relationship of these factors to impulsive and premeditated suicides.

Trauma

The extent of injuries sustained in alcohol-involved accidents, suicides, and suicide attempts may be influenced by the victims' drinking history or recent alcohol consumption. Intoxication is frequently found among trauma victims (Holt et al. 1980; Perrine 1975), and a history of trauma has been found to be a marker for the early identification of alcohol abuse (Skinner et al. 1984). In a recent review of studies on emergency room trauma cases, Roizen (1988) found that from 20 to 37 percent of all such cases involved alcohol.

Israel et al. (1980) found that the rate of occurrence of rib and vertebral fractures among alcohol-dependent persons was 16 times that in nondependent individuals. Data from health insurance claims also indicate a greater risk for fractures among alcohol-dependent drinkers (Holder 1988). Recent research has also found a dose-response relationship between a usual number of drinks consumed per occasion reported and the likelihood of fatal injury during a 9-year followup period (Anda et al. 1988).

Clinical findings suggest that both alcohol dependence and acute intoxication may be related to conditions that exacerbate the effects of trauma. For example, thrombocytopenia, a decrease in the number of blood platelets, has been related to alcohol ingestion in both alcoholics (Lindenbaum and Hargrove 1968) and nonalcoholics (Sullivan et al. 1977). Clinical studies have also shown reduced bone density in alcoholics compared to nonalcoholics (Saville 1975). Further, some bacterial infections are found more often in chronic alcoholics (Tillotson and Lerner 1967; Johnson et al. 1968; Manfredi et al. 1963), and intravenous administration of ethanol to nonalcoholics has been found to reduce bactericidal activity against certain bacteria (Johnson et al. 1969). Such findings, along with experimental results that indicate a potentiating effect of acute intoxication on standardized acute injuries in animals, predict a poorer prognosis for intoxicated individuals who have suffered a traumatic injury than for those who are not intoxicated (Waller et al. 1986; Maull 1988).

While most studies have reported that alcohol increases susceptibility to injury (Roizen 1988), clinical research on the relationship of alcohol and trauma have provided some conflicting evidence (Waller et al. 1986). In one study, hospitalized major trauma victims intoxicated at the time of injury were found to have a significantly lower mortality rate than nonintoxicated victims with similar severity of injury (Ward et al. 1982). Other studies have found no differences in outcomes of intoxicated and nonintoxicated drivers injured in motor vehicle accidents (Huth et al. 1983; Thal et al. 1985).

Waller et al. (1986) suggested that one possible reason why previous studies have failed to demonstrate a deleterious effect of alcohol on injury is that these studies included only individuals hospitalized after a crash and not those who died in the crash (Ward et al. 1982; Thal et al. 1985). This possibility is supported by the findings of a study that used data on deceased crash victims from State traffic safety and medical examiner records (Waller et al. 1986). Based on a mathematical model that controlled for accident type, intoxicated drivers were predicted to be 4.45 times likelier than nonintoxicated drivers to be killed in vehicle crashes that caused the least vehicle damage. Furthermore, intoxicated drivers were 3.31 times likelier to be killed than nonintoxicated drivers in crashes with intermediate vehicle damage and 1.83 times likelier to be killed in crashes with the most vehicle damage.

There is also evidence that injured individuals who are intoxicated when admitted to hospitals may be misclassified as more seriously injured than they actually are (Jagger et al. 1984). Waller et al. (1986) suggested that if such misclassified patients are matched for injury severity with nonintoxicated patients whose injury classifications are not skewed, the misclassified patients may appear to have a better recovery rate. In such instances, alcohol would falsely appear to have a protective effect on outcome (Waller et al. 1986).

Differential rates of BAC testing may also mask the relationship between alcohol and injury. Although Kraus et al. (1989) found that injury severity and hospital mortality were inversely related to BAC level among individuals who were hospitalized for or who died of brain injury, differential testing rates were also found for different levels of injury severity: 30 percent of mildly brain-injured persons were tested and 70 percent had a positive BAC; 74 percent of the moderately and severely injured were tested and 45 percent had a positive BAC. Moreover, among individuals with more severe injuries, BAC was directly related to neurological impairment at discharge and length of hospitalization.

Despite a significantly shorter time between injury and hospital admission, intoxicated patients with severe nonneurologic trauma were found by Elmer and Lim (1985) to have lower blood pressure and pCO_2 (indicative of hyperventilation) on hospital arrival than nonintoxicated patients. Although the hospital course did not differ for the two groups, the differences in blood pressure and pCO_2 indicate that intoxication can be a negative factor in trauma, especially if resuscitation is delayed (Elmer and Lim 1985).

Intoxication also influences the outcome for motorcyclists who are trauma victims. NHTSA's FARS data (NHTSA 1988a) indicated that, in 1986, motorcyclists involved in fatal crashes were more likely to be intoxicated than drivers of passenger cars or light, medium, or heavy trucks (see table 1). Intoxicated motorcyclists have been found to wear helmets one-third less frequently than those who were not intoxicated (Luna et al. 1984). Moreover, the protective effect of helmets was reduced for these individuals: Intoxicated motorcyclists wearing helmets sustained twice as many head injuries as nonintoxicated motorcyclists wearing helmets at the time of their accidents. Overall, critical head injuries were twice as likely to be fatal for intoxicated as for nonintoxicated motorcyclists, although the severity of injuries was similar for both groups (Luna et al. 1984).

Alcohol intoxication has also been shown to influence the outcome for pedestrians injured in motor vehicle accidents. Intoxicated pedestrians are three to four times likelier to be struck by automobiles than those who are not intoxicated (Irwin et al. 1983). A retrospective study of pedestrian accident victims admitted to a hospital trauma center during 1982 and 1983 (Jehle and Cottington 1988) revealed that 30 percent had been drinking. Ratings of injury severity, length of hospital stay, and frequency of injuries to the spine and chest were greater for patients who had consumed alcohol than for other injured pedestrians admitted to the hospital during this period. For further discussion on alcohol and trauma, see chapter VIII.

Crime and Family Violence

The belief in a link between alcohol and crime has a long history (Room 1983). The abuse of spouses by their partners and the abuse of children by their parents continues to be highlighted in the media and the clinical literature. Laboratory research has produced evidence of links between the pharmacologic effects of alcohol and aggressive behavior; that the relationship is complex, however, is suggested by findings indicating that expectancies about the effects of alcohol may influence aggressive behavior, and that cultural, environmental, and individual factors can influence the effects of drinking on aggression (laboratory research on alcohol and aggression is discussed in chapter IV). However, methodological weaknesses in much of the applied research conducted in these areas preclude firm conclusions about alcohol's role in specific types of violence.

Crime

It has been noted that prison populations have a high incidence of drinking problems and that people with alcohol problems are more likely to engage in criminal behavior than are people in the general population. Despite the apparent positive correlation between crime and alcohol, however, a direct causal relationship between alcohol and crime has not been established. Moreover, the majority of criminal offenders are not alcohol dependent, and the majority of alcoholics never commit serious crimes (Collins et al. 1981).

A number of factors may inflate the apparent relationship between alcohol and crime. Many investigations of this relationship have methodological limitations. Of 35 such studies reviewed by Greenberg (1981), only 5 were designed to control for the effects of age and sex—factors related both to the incidence of crime and to drinking. Intoxicated criminals also may be likelier to get caught (Roizen and Schneberk 1977) or convicted (Greenberg 1981) and thus likelier to be represented in prison populations. Statistics may also be distorted by practices such as plea bargaining, which allows a defendant to plead guilty to a lesser charge to avoid a full trial (Brain 1986).

Similarity in the relationship of age to alcohol use and to criminal activity has been suggested by two findings in the literature (Temple and Ladouceur 1986): (1) most serious crime in the United States is committed by youth and young adults, and (2) drinking also usually begins during or before adolescence and increases until the late teens or early twenties. However, the results of a recent longitudinal study conducted by Temple and Ladouceur (1986) of young men aged 16 to 31 suggest that this pattern of relationships is not found within individuals. While the degree of individual crime and alcohol use appeared to be related in adolescence, this relationship diminished with age, and by age 31 no significant relationship was found between an individual's criminal activity and alcohol use. Temple and Ladouceur (1986) believed that these findings suggest that, at most, any causal relationship between alcohol and crime is age specific.

The apparent relationship between alcohol use and criminal activity may reflect patterns of police activity as much as actual incidence of crimes. A study of first offenders in Scotland (Myers 1986) found that the majority of violent and nonviolent crimes occurred at or after pub closings in the afternoon and evening and that the largest number of these crimes occurred at night (see fig. 4). The investigator noted that when drinking establishments close, police are generally "on guard" to respond to behavior that may be unlawful or disturbing the peace. Individuals most likely to be apprehended for crimes in such circumstances also may be more likely to be intoxicated.

These findings indicate the importance of using an appropriate control group when assessing the relationship between alcohol and crime. As noted by Brain, "If 50% of the population of Glasgow are likely to be drunk on a Saturday night, the fact that perpetrators of criminal aggression are more likely to be drunk on this evening than on other days of the week becomes unimpressive as an indicator of a link between alcohol and aggression" (Brain 1986, p. 238). The limited use of appropriate control groups in research studying the relationship of crime and alcohol has deterred progress in understanding this relationship.

Family Violence

Research on family violence is also hampered by a number of problems (Leonard and Jacob 1988; West and Prinz 1987). These include the sensitivity of the issues involved, varying definitions of abuse, and frequent reliance on treatment and adjudicated populations for research samples. Furthermore, to the extent that a relationship between family abuse and alcohol can be documented, available data often do not make it possible to determine whether alcohol consumption is relevant or just coincidental to the circumstances that culminated in the abuse. Observational research studying families with alcohol-dependent members is a promising approach that may assist in achieving better understanding of alcohol's role in family violence.

Spousal Abuse

A recent review of studies using many methods and examining diverse samples supports clinical findings that many abused wives

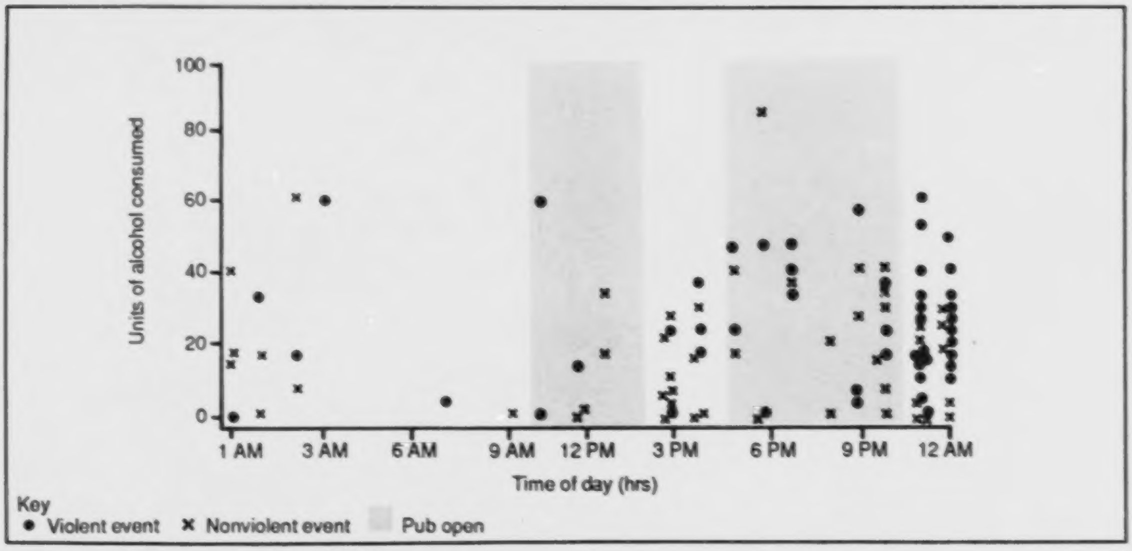

FIGURE 4. Offenders' self-reported alcohol consumption before violent and nonviolent crimes by time of day (N = 100).
SOURCE: Myers 1986. Copyright 1986 by Pergamon Press.

consider their husbands to be alcohol dependent or to have other alcohol-related disabilities (Leonard and Jacob 1988). Findings based on the responses of husbands also indicate a relationship between alcohol and physical abuse. Leonard et al. (1985) interviewed male factory workers about alcohol problems, wife abuse, level of marital satisfaction, and general level of hostility. Physical conflict with wives was acknowledged by 44 percent of those interviewed who met the diagnostic criteria for dependence and by 14 percent of those who did not. This relationship of alcohol and spousal abuse was maintained after marital satisfaction, hostility, and sociodemographic factors were controlled for. Another study compared alcohol use in couples characterized by physical abuse with use in couples who were maritally discordant but nonviolent and in couples who were satisfactorily married (Van Hasselt et al. 1985). Based on their self-reports and on their wives' observations, physically abusive males were found to have higher scores on a screening test for alcohol dependence than males in the two comparison groups.

A national telephone survey of more than 5,000 families in the United States found that the combination of blue-collar status, drinking, and approval of violence was associated with the highest rate of wife abuse (Kantor and Straus 1987). The probability of violence tended to increase with the frequency and amount of drinking. However, only 22 percent of the families reported that husbands were drinking immediately before their most recent episodes of abuse. Another study in a large Canadian city conducted diagnostic interviews of 1,200 randomly selected residents (Bland and Orn 1986). Residents who were diagnosed to be alcohol abusers or alcohol dependent, to have recurring depression, or to have an antisocial personality disorder were more likely to report physical violence toward their spouses.

The family and marital interactions of alcohol-dependent people have been a growing area of research interest in recent years. Observational studies of marital and family interactions in the home or in a homelike setting allow the manipulation of variables believed to be related to spousal abuse; this approach makes inferences of causal relationships between alcohol and spousal abuse possible (Leonard and Jacob 1988). Only a few such studies have been conducted, and none has actually focused on aggression or differentiated between violent and nonviolent couples. However, they have generated data relevant to the issue of alcohol and spousal abuse.

Studies using the observational approach have involved couples with one alcohol-dependent member who performs tasks requiring interaction. Verbal behavior and mood when sober and when intoxicated were observed. Two of these studies observed more negative responses and hostility by the couples under conditions of intoxication (Billings et al. 1979; Jacob et al. 1981), whereas in one study (Frankenstein et al. 1985) alcohol was related to more positive mood. The finding of more positive mood associated with drinking is consistent with the view that drinking may have positive and adaptive consequences for some couples with alcohol-dependent members by providing short-term solutions to familial problems (Steinglass 1981; Steinglass and Robertson 1983). In this view, such positive consequences may reinforce and thereby perpetuate excessive drinking.

Jacob and Leonard (1988) found that couples in which the alcohol-dependent member was an episodic drinker had patterns of interactions different from those of couples in which the alcohol-dependent member was a steady drinker. Alcohol-dependent men and their wives were observed during sessions when drinks were served and when no drinking occurred. During no-drinking sessions, the two members of each couple showed similar levels of negative behavior. During drinking sessions, husbands with episodic drinking patterns engaged in significantly more negative behavior than their wives, while steady-drinking husbands engaged in significantly less negative behavior than their wives. These findings suggest an association between general patterns of drinking behavior and the likelihood of negative behavior during a particular session of drinking.

Taken together, these studies suggest that alcohol may be associated with physical violence and other negative interactions in some families, but that in others, it may provide short-term solutions to problems and thereby perpetuate heavy drinking. Further understanding of the role of alcohol in spousal violence may be gained through a direct examination of the differential effects of alcohol and a placebo on interactions within violent and nonviolent couples (Leonard and Jacob 1988).

Child Abuse

In the relatively few studies of the relationship between child abuse and alcohol problems, a number of methodological and conceptual problems have been identified that may inflate or mask the degree of relationship.

Although the terms "child abuse" and "physical abuse" are frequently considered synonymous, other conceptually distinct classes of behaviors—including sexual abuse, incest, neglect, abandonment, and emotional abuse—also may be referred to as child abuse (Leonard and Jacob 1988). Studies may focus on one of these categories or combine data pertaining to more than one, thereby limiting the possibility of making comparisons across studies (Leonard and Jacob 1988). Studies often do not include a comparison group and are not designed to control for potentially confounding variables such as socioeconomic status (West and Prinz 1987).

The cases examined in these studies are frequently identified through treatment or social service programs. Such agencies may interpret behavior of a father not known to have a drinking problem differently from that of a father known to drink (Leonard and Jacob 1988). Similarly, a man who drinks heavily and abuses his children may be more likely to be labeled as alcohol dependent than a nonabusive father who drinks just as much (Leonard and Jacob 1988).

Most studies fail to use more than one simple measure of alcohol use, making it impossible to determine whether the apparent relationship between alcohol and child abuse is due to acute intoxication or to the debilitating effects of chronic alcohol use (Leonard and Jacob 1988). Most reports either do not state what criteria were used to determine alcohol dependence or do not describe the procedures used in assigning this label. They also do not discuss how intoxication at the time of child abuse was ascertained (Orme and Rimmer 1981).

A recent study has provided evidence supporting an association between alcohol problems and child abuse (Bland and Orn 1986). Standardized diagnostic interviews of randomly selected residents of a Canadian city found that female caretakers diagnosed as alcohol abusers or alcohol dependent, having recurrent depression, or having an antisocial personality were more likely to report that they had physically abused their children than parents without these diagnoses. This study also indicated that parents who abused their children also were more likely to report physical violence toward their spouses as well as involvement in other fights with adults and fights involving weapons (Bland and Orn 1986).

Although there are very few data supporting a causal connection between alcohol and child abuse, it must be emphasized that very little research has studied this relationship specifically and systematically. Consequently, firm conclusions about the nature of this relationship cannot be drawn.

Economic Costs of Alcohol Abuse

The adverse social consequences of alcohol dependence and abuse are associated with considerable economic cost. Assuming that the drinking pattern in the United States remains constant, the economic cost of alcohol abuse and dependence is projected to increase from $116.9 billion in 1983 to $136.3 billion in 1990 and $150.0 billion in 1995 (Harwood et al. 1985). This projected increase of 2 percent per year is based on expected population growth, the maturation of the "baby boom" generation, and growth in the productivity of the workforce. The projected values are in 1983 dollars and do not include the effects of inflation. Of the estimated $116.9 billion cost of alcoholism and alcohol abuse for 1983, nearly $71 billion (61 percent) was attributed to lost employment and reduced productivity and $15 billion (13 percent) to health care costs and treatment.

The economic cost of alcohol abuse in Minnesota in 1983 (Parker et al. 1987) was estimated between $1.4 and $2.1 billion—between 2.8 and 4.3 percent of the 1983 personal income in Minnesota and between 26 and 39 times the revenues generated by Minnesota's 1983 excise taxes on alcohol. The total health care cost in Minnesota in 1983 was $5.7 billion (Minnesota Department of Health 1984, cited in Parker et al. 1987). An estimated 3.4 to 6.4 percent of that amount ($195 million to $363 million) was attributed to alcohol-related medical costs, of which an estimated $107 million resulted from alcohol and combined alcohol and drug abuse treatment costs.

The cost of treatment services for 2 years for patients with a primary diagnosis of alcoholism in a New York county was compared with treatment costs for patients with other psychiatric diagnoses; results indicated that, although alcoholics represented the single largest diagnostic group (39 percent of the cohort studied), the cost of their care was only 22 percent of the total cost for services (Siegel et al. 1984). The lower treatment costs for alcoholics were attributed to fewer inpatient days and fewer days of the most costly full-day outpatient treatment services (see chapter XI for further discussion on treatment costs).

However, research has demonstrated that untreated alcoholics and their families have greater general health care costs than nonalcoholics and their families. A review of studies in this area (Holder 1987) indicated that, on the average, untreated alcoholics incur at least 100 percent higher general health care costs than nonalcoholics. This difference between untreated alcoholics and nonalcoholics increases over time before alcoholism treatment: During the 25 to 36 months before entering treatment, general health care costs for the untreated alcoholic are about 130 percent higher than for the comparable nonalcoholic, 180 percent higher during the 13 to 24 months before treatment, and 300 percent higher in the last 12 months before treatment. These differences are due primarily to substantially higher inpatient days per month per person for alcoholics (Holder 1987).

In addition to documenting higher health costs for untreated alcoholics, these studies demonstrate that alcohol treatment costs reduce general health care costs (Holder 1987). Although the largest reduction occurs in comparisons of the 12 months before and after treatment, studies have also found significant differences in health care costs in the 24 months before and after treatment begins (Holder 1987). Because the reductions in health care costs for alcoholics take place immediately after very large increases in costs, there is concern that the observed reductions may actually reflect regression to the mean (Holder and Blose 1986). To investigate this possibility, the pattern of health care costs of alcoholics who receive treatment would have to be compared with costs for those who do not receive treatment.

In a 6-year longitudinal study, all health care costs for a group of families with at least one member receiving alcohol treatment services were compared to costs of a matched group of families with no alcoholic members (Holder and Hallan 1986). The average monthly health care cost for the alcoholics' families was 1.5 to 21 times higher in all but the fifth year after treatment (see table 2).

A pattern of health care costs similar to that for alcoholism has been found for other chronic diseases, including the hypertensive, respiratory, diabetic, and ischemic heart disease groups (Schlesinger et al. 1983). Across all four disease groups, total health care costs were found to increase by as much as 500 percent during the 6 months before diagnosis, and total health care costs were found to drop sharply within the first year following diagnosis and the beginning of treatment (Schlesinger et al. 1983).

Summary

Alcohol has been implicated in the leading causes of accidental death in the United States: motor vehicle crashes, falls, and fires and burns. Of these, motor vehicle crashes are the leading cause of injury deaths, and approximately one-half were alcohol related in 1987. Although the proportion of all people killed in crashes in which at least one participant had a BAC of 0.10 percent or higher declined from 46 percent in 1982 to 40 percent in 1987, traffic crashes remain the greatest single cause of death in the United States for people between the ages of 5 and 34. It has

TABLE 2. Average monthly health care costs for alcoholics' families and nonalcoholics' families

Years before (-) and after (+) alcoholism treatment	Average monthly cost Alcoholics' families	Nonalcoholics' families
-2	$74.57	$ 6.54
-1	74.57	6.54
+1	40.72	1.90
+2	9.50	2.45
+3	24.27	3.80
+4	26.30	17.86
+5	12.18	16.63

SOURCE: Modified from Holder and Hallan (1986).

been estimated that the risk of a fatal crash, per mile driven, may be at least eight times higher for a drunk driver than for a sober one.

About 40 percent of all teenage deaths occur in traffic crashes. It is somewhat encouraging, at least from the perspective of alcohol involvement, that while the total number of fatal crashes for the age group increased 5 percent from 1982 to 1987, the number of fatal teenage crashes involving drunk drivers decreased 32 percent. Over all age groups, the proportion of intoxicated participants killed in fatal crashes has been declining. Nevertheless, approximately one-half of all crash fatalities are alcohol related.

Although less is known about alcohol involvement in other types of accidents, research findings suggest that alcohol increases the risk for falls, fires, and burns. The need for improvement in the measurement of alcohol's role in accidents has been emphasized; routine BAC testing in emergency rooms is needed, and development of a feasible means of measuring BAC at the scene of accidents could also reduce underreporting of alcohol involvement in accidents. One improvement in measurement is that appropriate diagnostic codes for indicating acute alcohol involvement at the time of an accident are forthcoming in ICD-10.

Research indicates that 20 to 36 percent of suicide victims have a history of alcohol abuse or were drinking shortly before their suicides, and that alcohol tends to be associated with suicides that are impulsive rather than premeditated. The percent of involvement in trauma is similar.

Although methodological problems in applied research investigating the relationships between alcohol use and crime and family violence preclude firm conclusions about alcohol's role, research does suggest that alcohol may be associated with physical violence and other negative interactions in some families; it has also been suggested that alcohol may provide short-term solutions to problems in some families and thereby perpetuate heavy drinking.

The economic cost of alcohol abuse and dependence is projected to increase from $116.9 billion in 1983 to $136.3 billion in 1990 and $150 billion in 1995.

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■ *Chapter VIII*

Diagnosis and Assessment of Alcohol Use Disorders

Introduction

The issue of the diagnosis of alcohol use disorders is linked closely with the problem of nomenclature and classification (Edwards et al. 1981). Successive efforts to develop reliable and effective classification systems and well-founded diagnostic procedures have led to many modifications of the terms used to describe these disorders.

The major trends in classification of alcohol use disorders in both clinical diagnosis and in research on diagnosis are discussed in the first section of this chapter. The diagnostic procedures are discussed in the second section.

Approaches to Classifying Alcohol Use Disorders

Principles and methods of diagnosis have evolved gradually and logically. They have tended to reflect the prevailing beliefs about the basis and nature of alcohol use disorders.

Two of the most influential approaches to defining and classifying alcohol use disorders in the past 20 years have been developed by the American Psychiatric Association (APA) and the World Health Organization (WHO) (Babor et al. 1986). Operational definitions and diagnostic criteria have been developed as part of these systems.

The pioneering definitions and diagnostic criteria proposed by the Criteria Committee of the National Council on Alcoholism (NCA) in 1972 were the first major attempt to make the diagnosis of alcoholism contingent on certain definite criteria. "Alcoholism," a term that has many meanings and has been used imprecisely by scientists as well as by the general public (Institute of Medicine 1987), was viewed as a progressive disorder in which physical consequences were emphasized. Any combination of 86 physiologic and clinical signs and behavioral, psychological, and attitudinal symptoms could qualify the patient for a positive diagnosis in this system (Babor et al. 1986). However, efforts to test the NCA criteria in a clinical setting, as reviewed by Jacobson (1980), were largely unsuccessful.

American Psychiatric Association

The first edition of the APA's *Diagnostic and Statistical Manual of Mental Disorders* (DSM) was published in 1952. Since then, this system has been revised several times and considerable changes have been made. The classification of substance abuse disorders in the third edition (DSM-III) (APA 1980) was influenced heavily by a series of clinical studies and published review papers on formal diagnostic criteria (Babor et al. 1986).

Initially, Guze et al. (1962) proposed basing a positive diagnosis of alcoholism on the existence of problems in at least three of five symptom groups: physical consequences (e.g., tremors, delirium tremens), frequent or heavy daily drinking, pathologic drinking behavior (e.g., inability to stop drinking, morning drinking), impaired social and occupational function (e.g., arrests, fights), and subjective evaluation by the patient or others that the patient is alcoholic. These criteria were modified later (Guze et al. 1969). In 1972 four of these groups (all except measures of daily consumption) were incorporated into the Feighner diagnostic criteria for use in psychiatric research (Feighner et al. 1972). In 1975 the Feighner criteria were published in slightly altered form as the Research Diagnostic Criteria (RDC) (Spitzer et al. 1975).

DSM-III contains a combination of the Feighner criteria and RDC as well as some significant innovations (Babor et al. 1986). In contrast to earlier editions of DSM, DSM-III includes alcoholism in a separate category of substance abuse disorders rather than as a subcategory of personality disorders, uses the term "alcohol dependence" in preference to "alcoholism," and uses specific behavioral symptoms and characteristics to distinguish between alcohol abuse and alcohol dependence. The diagnosis of alcohol abuse is based on the presence of regular abnormal consumption for at least 1 month and alcohol-related impairment of social or occupational functioning, whereas the diagnosis of alcohol dependence requires the additional involvement of tolerance or withdrawal symptoms. (Tolerance is the diminished effect of the same amount of alcohol that develops with regular use. Withdrawal is the development of a complex of symptoms when regular or sustained drinking is stopped abruptly or decreased.) Five independent dimensions or axes are used to provide a more comprehensive evaluation of the individual's condition. These DSM-III diagnoses were all-or-nothing decisions that did not allow for any gradation of severity.

World Health Organization

WHO has been a major force in formulating definitions of alcoholism since its establishment after World War II (Babor et al. 1986; Edwards et al. 1981). A series of WHO-sponsored expert committee meetings in which E. M. Jellinek participated produced first (in 1952) a broad definition of alcoholics as excessive drinkers with noticeable mental disturbance or interference with physical and mental health, interpersonal relations, and social and occupational functioning caused by alcohol dependence (WHO 1952). Then in 1955 the importance of physical criteria was emphasized and the major forms of alcohol dependence were characterized as inability to stop drinking before becoming drunk or inability to abstain from drinking due to the recurrence of withdrawal symptoms (WHO 1955). The 1952 and 1955 definitions were consistent with the definition of alcoholism (code 303) under "Other Nonpsychotic Mental Disorders" in the eighth edition of WHO's *International Classification of Diseases* (ICD-8) (WHO 1974).

In ICD-9, the next major revision of the WHO definition (WHO 1978), the term alcoholism was eliminated and the concept of alcohol dependence syndrome (ADS) was introduced. ADS was based on Edwards and Gross' (1976) formulation that a clinical syndrome of alcohol dependence, distinct from alcohol-related disabilities (physical, mental, and social dysfunction in which alcohol use is implicated), is recognizable. Both the disabilities and the dependence were considered dimensional phenomena (i.e., existing in degrees). ADS is described in terms of factors that characterize increasing severity of dependence. They are strong, internally felt needs to drink that have a psychophysiologic basis (Institute of Medicine 1987). Table 1 describes the seven criteria that constitute the ADS symptom complex.

The distinction between alcohol dependence and alcohol-related disabilities is a significant one that has been used in many studies of alcohol problems (e.g., Polich and Orvis 1979; Armor et al. 1981; Skinner 1985, 1988; Caetano 1985, 1987, 1988; and see Mandell's [1983] review). Many questionnaires have been developed to provide empirical support for the ADS construct; these questionnaires are discussed in the "Assessment" section of this chapter. Besides stimulating research, the ADS concept has helped bring some order and precision to alcoholism classification and nomenclature (Babor and Kadden 1985).

The major differences between the APA's DSM-III and WHO's ICD-9 were that (1) in ICD-9, ADS differentiated between alcohol dependence and alcohol-related disabilities, whereas alcohol-related disabilities could form

TABLE 1. Factors in the alcohol dependence syndrome

1. *Narrowing of the drinking repertoire:*
   Increasing severity of dependence is marked by increasingly stereotyped drinking with little day-to-day variability of beverage choice; drinking is scheduled so as to maintain a high blood alcohol level.
2. *Salience of drink-seeking behavior:*
   Increasing severity of dependence is marked by the individual granting highest priority to maintaining alcohol intake, with a failure of negative social consequences to deter drinking behavior.
3. *Increased tolerance:*
   Increasing severity of dependence is marked by the individual functioning at blood alcohol levels that would incapacitate the nontolerant drinker. In later stages, the individual begins to lose previously acquired tolerance because of liver damage, aging, and/or brain damage.
4. *Repeated withdrawal symptoms:*
   With increasing severity of dependence, the individual manifests more frequent and severe withdrawal symptoms; four key symptoms are tremor, nausea, sweating, and mood disturbance.
5. *Relief avoidance of withdrawal symptoms:*
   With increasing severity of dependence, the individual drinks earlier in the day and may even awaken in the middle of the night to drink.
6. *Subjective awareness of a compulsion to drink:*
   With increasing severity of dependence, the individual experiences a sense of "loss of control" or impaired control over alcohol intake and a subjective sense of craving or desire to drink. Cues for craving may include the feeling of intoxication, withdrawal, affective discomfort, or situational stimuli.
7. *Reinstatement after abstinence:*
   With increasing severity of dependence, the individual feels "hooked" within a few days of starting to drink and drinking will revert to the old stereotyped pattern. The six elements of the syndrome rapidly reappear.

SOURCE: Meyer 1986.

part of the definition of dependence in DSM-III, and (2) in ICD-9, ADS was a dimensional construct, whereas DSM-III dealt with alcohol dependence and abuse as "discrete categorical diagnoses" (Institute of Medicine 1987, p. 135).

An Emerging Synthesis: DSM-III-R, DSM-IV, and ICD-10

Changes proposed for the entire substance abuse disorders section of DSM-III (APA 1986; Rounsaville et al. 1986) were incorporated in the revised version DSM-III-R (APA 1987), which has been adopted widely, and the changes are being considered for inclusion in DSM-IV. Two primary changes were made: (1) A dimensional model of dependence resembling the ADS construct (with provision for denoting the degree of dependence as "in remission," "moderate," or "severe") was introduced; (2) The distinction between alcohol abuse and dependence was modified to put less emphasis on tolerance and withdrawal and to include cognitive and behavioral symptoms in the criteria for dependence. The same set of symptoms and behaviors is used to determine dependence on all classes of psychoactive substances. At least three criteria must be present to diagnose dependence (see table 2). Medical and social consequences are among the primary diagnostic criteria for alcohol

TABLE 2. Comparison of proposed ICD-10 and DSM-III-R diagnostic criteria (for alcohol use disorders)

Generic terminology	**Proposed ICD-10 criteria**	**DSM-III-R criteria**
Alcohol abuse	F10.1 *Harmful use of alcohol* a. Clear evidence that alcohol use is responsible for causing actual psychological or physical harm to the user. b. The nature of the harm should be clearly specified. c. The pattern of use has persisted for AT LEAST 1 MONTH or has occurred repeatedly over the previous 12 MONTHS.	a. A maladaptive pattern of alcohol use indicated by at least one of the following: (1) Continued use despite knowledge of having a persistent or recurrent social, occupational, psychological, or physical problem that is caused or exacerbated by alcohol use; or (2) Recurrent use in situations in which alcohol use is physically hazardous (e.g., driving while intoxicated). b. Some symptoms of the disturbance have persisted for at least 1 month, or have occurred repeatedly over a longer period of time. c. Never met the criteria for alcohol dependence.
Alcohol dependence	F10.2 *Alcohol dependence syndrome*	*Alcohol dependence*
	Three or more of the following are required:	a. At least three of the following are required:
Compulsion	i) A strong desire or sense of compulsion to drink.	[Partial relation to (1) below] (1) Alcohol often taken in larger amounts or over longer period than the person intended.
Loss of control	ii) Evidence of impaired capacity to control alcohol use behavior in terms of its onset, termination, or levels of use.	(2) Persistent desire or one or more unsuccessful efforts to cut down or control alcohol use.
Relief drinking	iii) Alcohol use to relieve or avoid withdrawal symptoms, and subjective awareness that this strategy is effective.	(9) Alcohol often taken to relieve or avoid withdrawal symptoms.
Withdrawal	iv) A physiological withdrawal state.	(8) Characteristic alcohol withdrawal.
Tolerance	v) Evidence of tolerance such that increased doses of alcohol are required in order to achieve effects originally produced by lower doses.	(7) Marked tolerance: need for markedly increased amounts of alcohol (i.e., at least a 50% increase) in order to achieve intoxication or desired effect, or markedly diminished effect with continued use of the same amount.

TABLE 2. Comparison of proposed ICD-10 and DSM-III-R diagnostic criteria (for alcohol use disorders) (Continued)

Generic terminology	Proposed ICD-10 criteria	DSM-III-R criteria
Narrowing of the repertoire	vi) A narrowing of the personal repertoire of patterns of alcohol use.	[None]
Progressive neglect	vii) Progressive neglect of alternative pleasures, behaviors, or interests in favor of drinking.	(5) Important social, occupational, or recreational activities given up or reduced because of alcohol use.
Consequences	viii) Persisting with alcohol use despite clear evidence of harmful consequences (see F10.1). Adverse consequences may be medical or psychological.	(6) Continued alcohol use despite knowledge of having a persistent or recurrent social, psychological, or physical problem that is caused or exacerbated by drinking.
Time with alcohol	[None]	(3) A great deal of time spent drinking or recovering from the effects of drinking.
Interference with role obligations	[None]	(4) Frequent intoxication or withdrawal symptoms when expected to fulfill major role obligations at work, school, or home, or when alcohol use is physically hazardous.
Time/duration	Symptoms experienced or exhibited AT SOME TIME DURING THE PREVIOUS 12 MONTHS or continuously during 1 MONTH.	b. Some symptoms of the disturbance have persisted for at least 1 month, or have occurred repeatedly over a longer period of time.

abuse, which is defined in DSM-III-R as a pattern of use that results in physical or psychological harm.

Like DSM-III, DSM-III-R uses five axes to provide a more comprehensive picture of the individual's condition. Rounsaville et al. (1987) suggested that with the elimination of the requirement for social consequences to have occurred as a result of substance use in DSM-III-R and with the expansion of the number of behaviors indicating impaired control over substance use, more individuals may fulfill the criteria for a substance abuse disorder and diagnosis may be established earlier.

At approximately the same time DSM-III-R was being planned, the concept of alcohol dependence in ICD-9 was being reviewed (WHO 1986). In the planned ICD-10, the APA and WHO systems have been synthesized somewhat, despite differences remaining in the wording, coverage, and application of the ADS concept (Caetano 1987, 1988; Rounsaville 1988). Both DSM-III-R and the planned ICD-10 define alcohol dependence similarly, based on the elements proposed by Edwards and Gross (1976), and both reflect a general evolution toward detailed evaluation of alcohol use disorders by means of multiple criteria (Babor et al. 1986). Table 2 compares ICD-10 and DSM-III-R criteria.

Both systems now contain a residual category that permits classification of the medical and psychological consequences that are directly related to alcohol consumption and associated with a regular pattern of use. The residual category included in DSM-III-R is intended for use with people who have relatively mild dependence or who have just begun to use a psychoactive substance (Rounsaville et al. 1987). ICD uses the term "harmful alcohol use," and DSM, "alcohol abuse," to denote consumption that is causing physical or psychological harm.

DSM-IV and ICD-10 most likely will be in worldwide use by 1994. It is hoped that they will lead to a consensus for diagnostic reimbursement and perhaps diagnostic research purposes.

Assessment

DSM-III-R and the proposed ICD-10 criteria allow for a diagnosis of alcohol dependence once an individual has three or more of the criteria listed in table 2. Because many combinations of indicators are possible, however, a positive diagnosis does not specify which kinds of problems brought a particular individual to treatment. Thus careful assessment before treatment becomes a necessity.

The APA and WHO approaches to classifying alcohol use disorders have generated abundant efforts to design assessment techniques and instruments that are effective in identifying persons (1) who are drinking excessively and experiencing alcohol-related disabilities but who may not fulfill established criteria for alcoholism and (2) who require minimal or more intensive treatment.

Advances in assessment technology have led to the development of procedures for screening, diagnosis, and differential assessment. A related development is Skinner's (1985, 1988, in press) proposal to transform the *bi*axial WHO classification—core ADS and physical/psychological/social disabilities associated with excessive drinking (Edwards et al. 1977)—into a *multi*axial classification that incorporates drinking history, dependence symptoms, medical and social problems related to drinking, and treatment-relevant individual factors.

Principles of Screening and Early Diagnosis

Screening is the use of easily and inexpensively administered procedures in an attempt to establish the presence/absence or degree of severity of a condition. It currently is undertaken for many physical and psychiatric disorders. Diagnosis is the confirmation of the nature and circumstances of a condition. It usually is accompanied by recommendations for intervention and treatment.

Screening is an important preliminary step in the diagnosis of alcohol use disorders. It is needed to ensure the early identification of individuals who have begun to develop or are at risk of developing alcohol use problems. Screening tests serve to direct these individuals toward further assessment, which may include a medical and psychiatric history, physical and psychiatric examinations, laboratory analysis, and further, more indepth assessment. Based on the assessment, a diagnosis is confirmed or refuted according to prevailing criteria (Saunders and Aasland 1987), such as DSM-III-R and ICD-9.

Strong support for the value of screening and early diagnosis is provided by numerous studies indicating the benefits of intervention and treatment for persons selected through the screening process. (See chapters X and XI.)

Screening procedures should be valid (i.e., measure what the researcher or clinician is attempting to measure) and yield findings that are reliable (i.e., consistent across raters and time). Other key properties of screening procedures are sensitivity and specificity. Sensitivity is a test's accuracy in identifying persons who have the target condition. Specificity is a test's ability to classify correctly as negative those who do not have the condition. As Rice (NIAAA 1987) pointed out, a perfect screening test would identify correctly all subjects with, and all subjects without, a given condition. However, this goal is unattainable, because a test's specificity decreases as its sensitivity increases and vice versa. Too much sensitivity would increase the likelihood of overdiagnosis of alcohol problems, and too much specificity would increase the chances for underdiagnosis. A balance is needed. Statistical techniques are used to select cutoff scores to classify subjects as positive or negative and to set the desired level of sensitivity and specificity of a given test.

Screening Methods and Standardized Interviews

Screening methods include questionnaires and interviews for assessing psychosocial indicators of alcohol problems, and laboratory tests and other biological measures for detecting biochemical markers of excessive drinking. Screening questionnaires are often self-administered. More complex instruments (questionnaires and standardized interviews) are used to reproduce the process by which clinicians arrive at a diagnosis and are checked for interrater reliability. Screening instruments typically do not provide information that is useful in selecting treatment programs and specifying treatment goals, whereas the more complex questionnaires and interviews collect richer information and permit more detailed evaluation of the patient with regard to treatment planning.

Many traditional screening questionnaires ask questions in "ever" terms to determine the presence or absence of symptoms. Other screening instruments require subjects to indicate present-state habits, behaviors, and feelings. Each type has advantages and limitations.

The CAGE questionnaire (Mayfield et al. 1974; Ewing 1984) is a simple, easily administered, four-item instrument named for the symptoms it seeks to detect: "Have you ever felt you should cut down on your drinking?" "Have people annoyed you by criticizing your drinking?" "Have you ever felt bad or guilty about your drinking?" "Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (eye opener)?" One "yes" response raises suspicions of an alcohol use problem, and more than one is a strong indication that a problem exists. CAGE takes only 30 seconds to administer. When included as part of a routine health screening it may detect alcohol use problems that might be missed otherwise (Clark 1981).

Bush et al. (1987) tested the hypothesis that the CAGE questionnaire would improve the rate of detection by physicians. More than 500 orthopedic and medical patients completed an interview containing CAGE. The findings show that physicians detected 63 percent of excessive drinkers and alcoholics without using CAGE, whereas with CAGE questions they identified 70 percent of excessive drinkers and 94 percent of alcoholics. (See also the "Primary Health Care Settings" section.)

The Michigan Alcoholism Screening Test (MAST) is a formal questionnaire (Selzer 1971) that can be administered during a regular health screening. Many of its items concern psychosocial complications of drinking and subjects' own perceptions of their alcohol problems. Originally designed as a face-to-face interview, it was converted first to a 25-item self-administered questionnaire (see table 3) and then to the 13-item self-administered Short MAST (SMAST) (Selzer et al. 1975). Pokorny et al. (1972) constructed a 10-item Brief MAST.

Cyr and Wartman (1988) interviewed 232 new patients in a medical primary care unit using a questionnaire that included the 25-item MAST. They concluded that incorporation of two questions—"Have you ever had a drinking problem?" and "When was your last drink?"—in the routine medical history is an important first step toward identifying patients who warrant further study to establish a diagnosis of alcoholism.

Similar to MAST is the Self-Administered Alcoholism Screening Test (SAAST) (Swenson and Morse 1975), an instrument that can be used as a questionnaire or interview. After using SAAST with 1,002 consecutive patients undergoing general examinations, Hurt et al. (1980) recommended this test, particularly as an adjunct to the physician's interview and examination. Results of administration of the original SAAST and a 9-item version to 520 alcoholics and 636 nonalcoholics strongly support the use of both versions in screening medical patients for alcoholism (Davis et al. 1987). Eighty percent of patients were classified accurately with the 9-item format as being alcoholic if they responded affirmatively to two items: "Do close relatives ever worry or complain about your drinking?" and "Have you ever felt the need to cut down on your drinking?"

The MacAndrew Alcoholism Scale (MacAndrew 1965) is a subset of items from the Minnesota Multiphasic Personality Inventory (MMPI) that appear to discriminate well between alcoholics and nonalcoholics. This scale was based on studies of the responses of 300 male alcoholic outpatients and 300 male nonalcoholic psychiatric outpatients from an urban treatment clinic. It is unique among self-report screening instruments in that it does not ask directly about drinking or its consequences. Although it is considered less valuable than other self-report procedures (Preng and Clopton 1986), it cannot be faked easily, and it may identify specific alcoholic subtypes (e.g., hedonistic, extraverted, and nonconformist) (Allen et al. 1988).

The Substance Abuse Proclivity Scale (SAPS) is an MMPI-derived scale that was developed with and for young males in the age range 16–21 (MacAndrew 1986). It is designed to detect problem-engendering use of alcohol and/or other substances. SAPS was shown to retain its effectiveness when applied to samples of young adult male substance abusers (ages 22–26), college students (22–26), psychiatric outpatients (22–26), and medical outpatients (20–29) (MacAndrew 1987).

Adolescent Drinking Index (Harrell and Wirtz 1988) is a self-report instrument developed specifically for use with adolescents. Its 24 items deal with four conceptual dimensions: loss of control of drinking; and social, psychological, and physical symptoms. In a recent study it correctly

TABLE 3. Michigan Alcoholism Screening Test (MAST)

Points		Question	YES	NO
	0.	Do you enjoy a drink now and then?	___	___
(2)	*1.	Do you feel you are a normal drinker? (By normal we mean you drink less than or as much as most other people.)	___	___
(2)	2.	Have you ever awakened the morning after some drinking the night before and found that you could not remember a part of the evening?	___	___
(1)	3.	Does your wife, husband, a parent, or other near relative ever worry or complain about your drinking?	___	___
(2)	*4.	Can you stop drinking without a struggle after one or two drinks?	___	___
(1)	5.	Do you ever feel guilty about your drinking?	___	___
(2)	*6.	Do friends or relatives think you are a normal drinker?	___	___
(2)	*7.	Are you able to stop drinking when you want to?	___	___
(5)	8.	Have you ever attended a meeting of Alcoholics Anonymous (AA)?	___	___
(1)	9.	Have you gotten into physical fights when drinking?	___	___
(2)	10.	Has your drinking ever created problems between you and your wife, husband, a parent, or other relative?	___	___
(2)	11.	Has your wife, husband (or other family members) ever gone to anyone for help about your drinking?	___	___
(2)	12.	Have you ever lost friends because of your drinking?	___	___
(2)	13.	Have you ever gotten into trouble at work or school because of drinking?	___	___
(2)	14.	Have you ever lost a job because of drinking?	___	___
(2)	15.	Have you ever neglected your obligations, your family, or your work for two or more days in a row because you were drinking?	___	___
(1)	16.	Do you drink before noon fairly often?	___	___
(2)	17.	Have you ever been told you have liver trouble? Cirrhosis?	___	___
(2)	**18.	After heavy drinking have you ever had Delirium Tremens (D.T.'s) or severe shaking, or heard voices or seen things that really weren't there?	___	___
(5)	19.	Have you ever gone to anyone for help about your drinking?	___	___
(5)	20.	Have you ever been in a hospital because of drinking?	___	___
(2)	21.	Have you ever been a patient in a psychiatric hospital or on a psychiatric ward of a general hospital where drinking was part of the problem that resulted in hospitalization?	___	___
(2)	22.	Have you ever been seen at a psychiatric or mental health clinic or gone to any doctor, social worker, or clergyman for help with any emotional problem, where drinking was part of the problem?	___	___
(2)	***23.	Have you ever been arrested for drunk driving, driving while intoxicated, or driving under the influence of alcoholic beverages? (IF YES, How many times? ___)	___	___
(2)	***24.	Have you ever been arrested, or taken into custody, even for a few hours, because of other drunk behavior? (IF YES, How many times? ___)	___	___

*Alcoholic response is negative.

**5 points for Delirium Tremens.

***2 points for *each* arrest.

SCORING SYSTEM: In general, five points or more would place the subject in an "alcoholic" category. Four points would be suggestive of alcoholism, three points or less would indicate the subject was not alcoholic.

SOURCE: Lettieri et al. 1985.

identified 88 percent of adolescents with, and 82 percent without, alcohol problems when these two categories were distinguished (Allen et al. 1988). The Ten Question Drinking History was developed to identify heavy drinking among obstetric patients (Rosett and Weiner 1985).

The Addiction Severity Index (McLellan et al. 1980) is a highly structured clinical interview designed for use by a trained technician to rate the severity of problems in six areas that suggest the need for treatment: drug and alcohol use, medical, psychiatric, legal, family and social, and employment and support. Subjects' status during the previous 30 days is a major focus. Studies conducted with male veteran alcoholics and drug addicts (McLellan et al. 1980), male and female opiate addicts seeking treatment (Kosten et al. 1983), and male and female drug- and alcohol-dependent clients (NIDA 1985) have shown it to be an effective instrument for differentiating adults and self-supporting, older adolescents into subgroups with different treatment needs.

The Inventory of Drinking Situations is a self-report questionnaire that provides a profile of the types of situations in which a client drank heavily during the previous year (Lettieri et al. 1985). It is intended for use at the beginning of therapy and at followup.

Numerous questionnaires have been developed to provide measures of the degree of alcohol dependence in accordance with Edwards and Gross' (1976) original ADS formulation. These include the Severity of Alcohol Dependence Questionnaire (Stockwell et al. 1979, 1983), Edinburgh Alcohol Dependence Schedule (Chick 1980a,b), Alcohol Dependence Scale (Skinner and Allen 1982; Skinner and Horn 1984), Last Six Months of Drinking Questionnaire and Last Month of Drinking Questionnaire (Hesselbrock et al. 1983, 1985), Rand Dependence Scale (Polich et al. 1981), and Short-Alcohol Dependence (Raistrick et al. 1983), which also is called the Alcohol Dependence Data Schedule (Edwards 1986). Skinner's (1981b) analysis of the scales of the Alcohol Use Inventory (Wanberg et al. 1977), an instrument used to determine quantity and frequency of alcohol consumption at screening and followup, also provides empiric evidence for the ADS construct.

At least three structured interviews have been developed recently to evaluate the diagnostic criteria for ADS and currently are being field tested: the Structured Clinical Interview for DSM-III-R, devised by Spitzer and Williams; the Composite International Diagnostic Interview (CIDI), devised by Robins et al. (1988); and Schedules for Clinical Assessment in Neuropsychiatry (SCAN) (Wing et al. in press). CIDI was created at the request of the WHO task force formed to help write the forthcoming ICD-10 chapter on mental disorders. CIDI is an international epidemiologic survey instrument that permits DSM-III-R and ICD-10 to be derived by computer from the results of a questionnaire administered by a nonclinician. SCAN is an expanded version of the ninth edition of the Present State Examination, an interview designed to allow an examiner to determine the presence and severity level of neurological, cognitive, and psychosocial symptoms of mental disorders. It contains a new section devoted to alcohol use disorders. Multicenter field trials are under way.

Table 4 provides examples of assessment instruments designed to achieve a variety of goals in the recognition and treatment of alcohol problems. Table entries are intended as examples only and should not be construed as necessarily the best instruments available.

Self-Report Procedures

Self-report procedures (e.g., interviews, questionnaires, and computer-assisted tests) have been the main method used to assess drinking behavior and related consequences. The relative validity and reliability of responses have been issues of concern.

Sobell, Sobell, Riley, et al. (1988) found that 69 excessive drinkers' retrospective reports of past drinking behavior and life events (approximately 8 years prior to interview) were generally reliable. The investigators assessed drinking behavior with the Lifetime Drinking History Questionnaire (Skinner and Sheu 1982) and life events with the Recent Life Changes Questionnaire (Rahe 1975).

Davis and Morse (1987) reported a high level of agreement on SAAST results for 240 patient-collateral pairs, thus confirming Morse and Swenson's (1975) finding that collateral SAAST ratings of patients' drinking behavior are accurate and can be helpful in alcoholism diagnosis.

A number of factors can influence respondents' performance, and response bias can have many sources. Skinner (1984) composed a checklist of specific factors affecting the validity of alcohol use assessments (see table 5). Table 6 lists various procedures that may be used to reduce response bias and increase validity that have been developed in a series of studies on measurement

TABLE 4. Examples of assessment instruments used for screening, diagnosis, and treatment planning in alcohol use disorders

Name of instrument / Instrument characteristics	Who administers				Type			Setting				Specific target population		Computer-assisted	
	Self	Clinician	Nonclinician	Administration time	Questionnaire	Unstructured interview	Structured interview	Screening	Intake	In-treatment	Follow-up	Adolescents	Adults	Administration	Scoring
Pencil-and-paper measures (overt content)															
1. CAGE	x	x		1 min	x	x		x					x		
2. History of Trauma	x	x		1–2 min	x	x		x					x	x	
3. Michigan Alcoholism Screening Test	x	x		15 min		x		x					x		
4. Adolescent Drinking Index	x			5 min	x			x				x			
Pencil-and-paper measures (latent content)															
5. MacAndrew Scale	x			up to 90 min	x			x			x		x	x	
6. Substance Abuse Proclivity Scale		x		up to 90 min	x			x					x		
Combined written, clinical, laboratory measures															
7. Alcohol Clinical Index	x	x		5 min	x	x		x					x		
8. Alcohol Use Disorders Identification Test	x		x	3 min		x		x					x	x	
Diagnostic measures															
9. Diagnostic Interview Schedule, alcohol section			x	10 min			x		x		x		x		x
10. Composite International Diagnostic Interview			x	10 min			x		x		x		x		x
Measures of severity of dependence															
11. Alcohol Dependence Scale	x			5–10 min	x	x		x	x		x	x	x		
12. Severity of Alcohol Dependence Questionnaire	x			5 min	x				x		x		x		
13. Edinburgh Alcohol Dependence Schedule			x	15–25 min		x		x	x		x		x		
Measures to assess drinking pattern/beliefs															
14. Alcohol Use Inventory	x		x	30–40 min	x			x			x		x		
Measures to assist in choice of treatment:															
15. Addiction Severity Index			x	30–40 min			x	x	x		x		x		
16. Inventory of Drinking Situations	x			10 min	x			x		x	x		x		

TABLE 5. Factors influencing the validity of self-reports

Invalidating factors	Validating factors
• Individual has positive blood alcohol concentration at time of assessment.	• Individual is alcohol (or drug) free at time of assessment.
• Individual is experiencing withdrawal symptoms or acute physical/mental distress.	• Individual is stable, no major symptoms.
• Unstructured, general, or vague items are used in taking the drinking history.	• Structured, carefully developed instruments are used.
• Individual is not aware that self-reports will be checked against objective criteria.	• Individual is aware that self-reports will be checked with other sources (laboratory tests, collaterals, records).
• Thre is minimal contact or supportive counseling with the individual.	• Good rapport is established with the individual.
• Individual has clear motives to dissimulate, e.g., abstinence is a condition of parole or continued employment.	• Individual has no obvious reasons for distorting reports of alcohol use.
• Individual has doubts about the confidentiality of information he or she provides.	• Confidentiality of information is assured to the individual.

SOURCE: Modified from Skinner 1984.

of response bias and interviewer bias (Bradburn and Sudman 1979; Cannell et al. 1981; Cooper et al. 1981; Harrell 1985; Hubbard et al. 1977; Skinner 1981a).

Until recently, the methods used most often to evaluate drinking behavior have been quantity-frequency methods, which require individuals to characterize their drinking in terms of average or typical consumption patterns. The timeline (TL) method, an alternative for assessing recent drinking behavior, requires subjects to estimate their actual daily alcohol intake for a specified period. With the use of the TL method, generally good agreement has been found between self-reports and collaterals' reports of drinking (Maisto et al. 1979, 1982, 1985; O'Farrell et al. 1984; Zweben 1986) and between official reports and self-reports of arrests and hospitalizations (Cooper et al. 1981; Maisto et al. 1979, 1985). The TL method has been shown to be valid in a nonclinical population as well (Connors et al. 1985; Sobell et al. 1986; Sobell, Sobell, Leo, and Cancilla 1988).

O'Farrell and Maisto (1987) summarized the conclusions of a number of literature reviews on the reliability and validity of alcoholics' self-reports of drinking and related behavior (mainly Marlatt et al. 1986 and Sobell et al. 1986; also Armor et al. 1978; Babor et al. 1986; Maisto and Cooper 1980; Midanik 1982; O'Farrell and Langenbucher 1988; Polich 1982; Skinner 1984; Sobell and Sobell 1982). They indicated good reliability and validity across different samples of excessive drinkers for frequency reports of hospitalization, jailing, drinking, and abstinence, and good reliability and modest agreement with collaterals' reports for measures of problem severity and alcohol dependence symptoms. For amount consumed, reliability is good for outpatient alcoholics but not for inpatient and residential alcoholics, and substantial agreement with collaterals' information is found only for problem drinkers at followup assessment.

Computerized Screening

Skinner and Pakula's (1986) brief survey of the literature on the impact of computerization on psychometric properties indicates that computerized test administration may standardize the assessment situation, increase the accuracy of information about sensitive issues, and reduce response bias. However, it also may present an environment that is different from the standard procedure for test administration and may introduce unreliability for individuals who are unfamiliar with computers.

The potential for innovative use of computerized assessment is considerable. Skinner et al. (1985a, 1987) studied the possibility of using microcomputers to screen family practice patients. Information about alcohol, tobacco, and other drug use was elicited with a self-

TABLE 6. Procedures for minimizing response bias and enhancing validity

Source of bias	Solution
Ambiguous role requirements or task definition	Guarantee anonymity/confidentiality
	Give clear instructions/examples
	Emphasize scientific or clinical role
Specificity of desired responses	Word questions carefully
	Use multiple questions
	Ask followup questions
Interviewer bias and unreliability	Train interviewer
	Standardize interview protocols
	Develop specific interview techniques
Forgetting, telescoping	Increase question length
	Provide more complete instructions
	Give fixed-response choices
	Use memory aids and bounded recall techniques[a]
Response distortion	Alert subject to the problem
	Pose recognition questions
	Use diaries/calendars/timeline
Motivation	Obtain a clear commitment/agreement
	Give clear instructions
	Use bounded recall techniques[a]
	Provide prompts/encouragement/reinforcement
	Give a feedback session
	Use the "bogus pipeline procedure"[b]

[a] A technique whereby subjects are given results of previous responses to aid their recall.

[b] A procedure in which subjects are asked to give information and led to believe that the person collecting the information can validate it through objective, external means.

SOURCE: Modified from Babor et al. 1987. Copyright 1987 by Alcohol Research Documentation, Inc., Rutgers Center of Alcohol Studies.

administered questionnaire, an interview conducted by a research assistant, or computerized assessment. No differences in levels of consumption or reported problems were found among patients in the three assessment conditions. Before screening, most patients indicated assessment by interview as their first choice and computerized assessment as their last choice. After screening, however, computer-assessed patients indicated significantly increased preference for this method (from 13 to 43 percent). Skinner et al. (1987) found patients' responses to computerized assessment to be reliable over a 3-week period and consistent with responses given to their physician.

Patients being treated by psychiatrists also seem to accept computer interviews well (Coddington and King 1972). Research has shown that this approach can produce more accurate and reliable information than a clinician elicits (Carr and Ghosh 1983; Carr et al. 1981). Patients also tend to reveal more to the computer than to a psychiatrist (Greist, Gustafon, et al. 1973; Greist, Klein, et al. 1973; Evans et al. 1973; Lucas et al. 1977), especially about deviant social behavior (Greist 1977), perhaps because they perceive the computer to be nonjudgmental (Greist, Gustafson et al. 1973).

Biochemical Markers

Laboratory tests frequently are used to corroborate the results of the physician's interview and examination and of self-administered tests. Laboratory findings can represent objective biochemical markers of problem drinking and alcoholism in uncooperative patients who deny any drinking problem (Reich 1988).

Allen et al. (1988) distinguished two basic approaches to identifying biochemical markers of alcoholism. The first relies on routinely administered clinical laboratory tests, and the second, on specialized laboratory tests.

Researchers have achieved varying degrees of success using conventional laboratory markers alone to identify and monitor alcohol abusers; some of these markers are blood levels of gamma-glutamyltransferase (GGT), aspartate aminotransaminase/glutamic oxaloacetic transaminase, and alkaline phosphatase (all enzymes found in the liver and other organs); mean corpuscular volume (MCV; an index of red blood cell size); uric acid; blood lipids; and blood alcohol concentration (BAC) (Salaspuro 1986). Values of these markers increase to varying degrees with alcohol use.

The usefulness of GGT, which is involved in the active transport of amino acids across the blood-brain barrier, has been the subject of much study. This enzyme has been found to be a relatively sensitive index of liver damage compared with other routinely assayed enzymes (e.g., the transaminases, bilirubin, and albumin) in clinical studies of alcoholics and heavy drinkers (Schuckit and Griffiths 1982; Gjerde et al. 1987). Penn and Worthington (1983) questioned the clinical relevance of increased GGT activity in the blood, because serum activity of this enzyme rises in almost all types of liver disease and may rise in pancreatic, cardiac, and kidney diseases, neurologic disorders, and diabetes mellitus, among other diseases. Moreover, serum activity of GGT is affected by various substances, including alcohol. Based on studies of Norwegian subjects, Gjerde et al. (1987) suggested the possibility of using GGT as an epidemiologic marker of alcohol consumption, but they emphasized the need for caution in applying their findings to populations from other countries. Irwin et al. (1989) found an association between increased blood GGT levels and impaired visuoperceptual and visuoconceptual functioning in 132 chronic alcoholic men in an alcohol treatment program. Other laboratory tests documenting liver injury (aspartate aminotransaminase and alanine transaminase, total and direct bilirubin, albumin, and globulin) did not predict neuropsychological performance or contribute significantly to the specific association between elevated GGT levels and neuropsychological deficits. Another potential marker is urinary dolichols (substances involved in the formation of certain protein-carbohydrate compounds), which have been reported to be significantly more sensitive than GGT for detecting alcoholism (Roine et al. 1987).

Simultaneous use of two or more conventional laboratory markers generally has proven more successful than use of a single marker. O'Farrell and Maisto (1987) cited findings indicating that the level of marker sensitivity ranges from a low of 30 to 40 percent when a single individual biochemical is used with healthy alcoholics, to a high of 70 to 80 percent when two or more markers are used with alcoholics receiving treatment for alcohol-related health problems (Bernadt et al. 1982; Chick et al. 1981; Sanchez-Craig and Annis 1981; Skinner et al. 1984).

Watson et al. (1986) reviewed studies demonstrating that the use of statistical analysis of pattern changes in laboratory test batteries increases the diagnostic efficiency of biochemical markers. There is no consensus yet regarding which statistical model applies best to the diagnosis of alcohol use disorders by routine blood tests (e.g., Eckardt et al. 1984; Freedland et al. 1985).

Excessive alcohol consumption has been associated with increasing levels of the carbohydrate-deficient form of transferrin, a protein that transports iron. Analysis of carbohydrate-deficient transferrin (CDT) with a new technique permitting rapid detection and measurement in serum indicated that CDT may be a clinically useful marker of heavy alcohol consumption (Stibler et al. 1986). Clinical evaluation showed that 77 patients with alcohol use disorders could be distinguished from 33 total abstainers and from 80 healthy normal consumers with a specificity of 100 percent and a sensitivity of 91 percent. CDT levels correlated significantly with the amount of alcohol consumed during the preceding month. Elevated CDT levels appeared occasionally in healthy subjects after daily consumption of approximately 60 g of alcohol (about 2 oz) during a 10-day period. Thus it appears that, to produce a general elevation of CDT value, either the consumption level has to be higher or the period of regular intake has to be longer.

Stibler and Hultcrantz (1987) studied the specificity of the new technique with respect to liver diseases of nonalcoholic origin. CDT values were normal in all 87 patients who did not have current excessive alcohol consumption, regardless of their type or degree of liver disease. Thirteen of the 15 heavy drinkers (87 percent) who were currently consuming 60 g of alcohol or more daily showed elevated CDT values, but levels were normal in patients with alcohol-induced liver disease who had stopped drinking many years earlier. Thus CDT can be used to assess present but not previous heavy consumption, even in patients with various liver diseases.

Behrens et al. (1988) demonstrated the effectiveness of CDT in identifying black and Puerto

Rican alcoholics. Elevated CDT levels also were found in this study in some nonalcoholics with primary biliary cirrhosis (chronic bile duct inflammation resulting in fibrosis of the liver and spleen).

Use of the blood level of the mitochondrial liver enzyme aspartate aminotransferase (AST) and its ratio with total AST has been found effective in discriminating between alcoholics and normal subjects and in detecting chronic excessive drinking (Nalpas et al. 1984, 1986; Lumeng 1986). The blood metabolite 2,3-butanediol (Rutstein et al. 1983) has been proposed as a possible marker of alcohol use disorders.

Numerous studies have focused on the use of acetaldehyde (ACH), the major metabolite of alcohol. All known pathways of alcohol metabolism result in producing ACH (Lieber 1988b). ACH has been shown to bind to certain proteins and to form acetaldehyde adducts (AAs) (Lieber 1988a,b; Nomura and Lieber 1981; Behrens et al. 1988; Lin et al. 1988; Donohue et al. 1983; Stevens et al. 1981). Researchers have investigated the potential use of AAs as a marker of alcohol consumption (Hoerner et al. 1986; San George and Hoberman 1986; Niemelä et al. 1987; Hoerner et al. 1988; Petersen et al. 1988). The antibodies against AAs, formed either by immunization with the AAs or by chronic alcohol consumption, also may have diagnostic relevance (Israel et al. 1986, 1987). Israel et al. (1988) reviewed the concepts involved in the immunologic abnormalities accompanying alcoholic liver disease. They emphasized recent findings that support a possible role of alcohol metabolites in triggering an immunologic response and the potential use of antibodies against ACH-generated epitopes (antigenic determinants) in diagnosing alcoholism and alcoholic liver disease. (See chapter V.)

The new findings concerning the role of ACH-protein adducts and associated immune response in the development of alcohol-induced liver injury have implications for diagnosis and followup of alcohol use disorders. This area is one of the most active areas of research today.

Self-Reports Versus Biological Markers

Despite problems with self-administered tests, they generally are more sensitive and specific than routine blood tests and probably will continue to be for some time (Allen et al. 1988). Known heavy drinkers may be less likely to misrepresent their drinking problem. When alcohol problems are not apparent, self-report is preferable to other measures, because specificity is higher. Self-report alone is not an ideal tool for followup, however (e.g., Orrego et al. 1979; Fuller et al. 1988).

O'Farrell and Maisto (1987) reviewed studies of the relative contribution of biochemical markers and other methods. They cited findings showing the clear superiority of MAST, SMAST, CAGE, and another instrument, the Reich test, to GGT measurements in identifying known alcoholics (Bernadt et al. 1982, 1984; Peterson et al. 1983). Bell and Steensland (1987) compared the use of GGT activity and Brief MAST and CAGE results to predict estimated alcohol consumption in patients admitted to a clinic for alcoholics. GGT was not as sensitive as the questionnaires. Bush et al. (1987) found that CAGE had much greater sensitivity than MCV, GGT, and liver transaminase values as a screening test for excessive alcohol consumption with orthopedic and medical inpatients and that using CAGE questions improved physicians' rates of detection. Morse (NIAAA 1987) reported that SAAST has proved more sensitive than laboratory tests in comparison studies conducted with alcoholic inpatients.

Lumeng (1986) recommended the joint use of GGT measurement and one or more self-administered tests to enhance assessment objectivity. To improve diagnostic value, Watson et al. (1986) proposed using two brief personal history instruments, CAGE and the five-item History of Trauma (Skinner et al. 1984), in conjunction with the most effective laboratory tests. Yates et al. (1987) indicated that the combination of BAC measurement and a questionnaire is more accurate than BAC measurement alone in detecting the majority of heavy drinkers in an accident and emergency department. Their results support the suggestion that many problem drinkers, who may be dangerous drivers, go undetected when BAC is the only screening tool (Dunbar et al. 1983).

A seven-item computerized biochemical and hematologic profile devised by Beresford et al. (1982) correctly identified 79 percent of alcoholic patients and 80 percent of nonalcoholic patients among admissions to the medical service of a county teaching hospital.

In general, biochemical tests currently are a valuable tool for the use of hospital-based physicians in detecting hidden alcohol use disorders. Several questionnaires, however, have been shown to be more sensitive than biochemical tests, and joint administration of self-report and laboratory measures has been suggested.

Combination Instruments

Because each type of assessment method has some limitations affecting sensitivity and specificity, screening tests combining self-report, clinical examination, and blood tests have been designed. Multimodal assessment is consistent with Skinner's (1985) multiaxial classification of alcohol problems.

Skinner et al. (1986) demonstrated that certain clinical findings can be used to complement psychosocial or laboratory data to improve the rate of detection of excessive drinking. They used 108 clinical and laboratory tests to examine 131 outpatients with alcohol problems, 131 social drinkers, and 52 family practice patients. Findings from clinical examination were more valuable than laboratory data for diagnosing excessive drinking. A set of 17 clinical signs and 13 medical history items that could discriminate outpatients with alcohol problems from social drinkers and family practice patients was formed into the Alcohol Clinical Index (ACI). In practice this instrument has been shown to outperform laboratory data when used by experienced clinicians in the alcohol research field, but its value in the hands of hospital physicians remains to be demonstrated. Skinner and Holt (1987) recommended administering ACI during clinical examination and corroborating its results with brief self-report questionnaires on alcohol consumption and alcohol-related problems.

A new combination instrument for the early detection of individuals whose alcohol consumption is potentially harmful has been developed and validated as part of a WHO collaborative project (Saunders and Aasland 1987). A multiaxial assessment tool, the WHO Composite Diagnostic Instrument, was administered to groups of alcoholic and nonalcoholic patients in six countries. General subject information was obtained, and questions were asked about medical symptoms often associated with excessive drinking (subjective complaints and history of trauma), consumption level, drinking habits, social consequences, and self-perception of alcohol problems. Clinical signs that have been found to be important in detecting alcohol problems (e.g., tremor of the hands, lips, and tongue; physical appearance of the skin, tongue, and mucous membranes; presence of liver enlargement; and hypertension) were assessed mainly with items from the instrument developed by the French physician Le Gô, which was based on screening of more than 1 million French railway workers (Le Gô 1976). Laboratory tests included serum GGT, serum AST, serum alanine aminotransferase, serum high-density lipoprotein-cholesterol, BAC, and MCV.

The main screening instrument devised from this study is a 10-item questionnaire that attempts to identify early-stage problem drinkers (Babor et al. 1989). It is called the Alcohol Use Disorders Identification Test (AUDIT). AUDIT is simple, inexpensive, transportable, designed for self-administration or administration by an interviewer with minimal training, equally applicable to screening large populations or to case detection in a clinical setting, and short enough to be used in the lifestyle assessment procedures devised by Skinner et al. (1985a,b). It is adaptable for presentation by microcomputer, thereby permitting a decision about intervention to be made before the subject leaves.

Sites for Screening of Alcohol Problems

Many settings in the health care system have been proposed as appropriate for identifying alcohol use disorders early.

Primary Health Care Settings

The primary care physician, who is usually the first care provider to see patients with medical problems associated with excessive use of alcohol, is in a key position to make early diagnoses (Lewis 1989). However, primary care physicians frequently underdiagnose these problems or underreport recognized problems. In a study of general practitioners, Clement (1986) found that alcohol-related problems often are neither diagnosed nor attended to in primary care settings. Brown et al. (1987) used a computer-simulated encounter with an alcoholic patient to determine the diagnostic performance of primary care physicians. Of the 95 physicians studied, 32 percent diagnosed alcoholism with maximum certainty, 27 percent erroneously diagnosed other psychiatric problems (usually anxiety or depression), and 41 percent said no psychosocial diagnosis was very likely.

Missed diagnosis may be related to three factors: (1) the coexistence of alcohol use disorders and psychiatric disorders in the same individual, (2) stereotypes regarding heavy drinkers and alcoholics, or (3) inexperience. (See chapters II and XI for more information on psychiatric comorbidity.)

First, coexistence of alcohol use disorders and psychiatric disorders can complicate screening and diagnosis. Such comorbidity is not uncommon. The example of affective disorder is illustrative. Finlayson et al. (1988) reviewed the medical records of 216 patients between 65 and 83 years old who had been hospitalized for alcoholism (Mayo Clinic sample) and found affective disorder in 12 percent. Schuckit (1986) suggested that alcoholism and major affective disorder are independent diseases with some overlapping clinical symptoms. Family history may help clarify the nature of the relationship between alcoholism and affective disorders (Zisook and Schuckit 1987).

Blankfield (1986) found that detoxification is essential before transient and enduring psychiatric manifestations can be distinguished in alcohol-dependent inpatients. She studied 50 consecutive patients admitted with grief, agoraphobic, paranoid, and depressive symptoms related to alcohol withdrawal. These symptoms disappeared with detoxification, while other symptoms constituting syndromes persisted.

The coexistence of dementia and alcohol use poses special diagnostic problems in older people. Dementia associated with alcohol disorders needs to be distinguished from the dual disorder of senile dementia of the Alzheimer type and coexisting alcohol use disorders (Atkinson 1988).

Finlayson et al. (1988) found that stressful life events more frequently preceded admission for patients with late-onset alcohol problems (at age 60 years or later) than for patients with early-onset problems (before age 60). They emphasized that physicians caring for older patients should include questions about the occurrence of major life events in their assessments of the possibility of alcohol use disorders.

Substantial alcohol-related morbidity is "hidden" among older Americans, partly because of the inadequacy of current screening and diagnostic methods for this population (Stinson et al. 1989). Graham (1986) suggested that (1) self-reports of alcohol consumption may be particularly inaccurate in this group because of memory problems, difficulties in "mental averaging," and high levels of denial of unfavorable traits; (2) the traditional cutoff scores used for defining heavy consumption may be inappropriate in older patients because of their increased sensitivity to alcohol; (3) assessment scales that were validated with younger populations may be unsuitable for older people, who have different lifestyles and different problems; and (4) symptoms often recognized as signals of alcohol use disorders may be attributed to dementia or other illnesses in older people.

Second, erroneous stereotypes may prevent physicians from recognizing alcohol problems in their patients (Schuckit 1987). Coulehan et al. (1987) suggested that clinicians may be inclined to stereotype alcoholics and excessive users of other drugs as persons who have the characteristics considered diagnostic criteria for antisocial personality disorder (e.g., inability to sustain consistent employment, impulsivity, recklessness, irritability, aggressiveness, failure to honor financial obligations, and inability to maintain enduring relationships or function as responsible parents). Their study took place during an 18-month period in three academic primary care settings—two family health centers and an internal medicine clinic. Among 294 adult patients, primary care physicians identified 17 (40 percent) of the 42 patients who were diagnosed by a structured psychiatric interview (Diagnostic Interview Schedule) as suffering from excessive alcohol or other drug use. Clinically identified patients were more likely to be older and married, to use multiple drugs, and to have antisocial personality disorders, whereas patients who were not identified clinically were more likely to have a coexisting depressive disorder.

Third, medical residents may have problems diagnosing alcohol use disorders in an outpatient medical setting. Moore and Malitz (1986) compared the responses of 95 patients to the CAGE questionnaire with residents' diagnoses of alcoholism on the medical record. Residents diagnosed alcoholism in only 11 (55 percent) of the 20 patients who had answered "yes" to three or more CAGE questions and only 14 (45 percent) of the 31 patients who had given two or more "yes" answers. They diagnosed alcoholism correctly only when aspartate transaminase and MCV were elevated. (Aspartate transaminase is elevated only when signs of physical damage or dependence are present. MCV elevation is not indicative of organ damage; this marker has good sensitivity at low levels of consumption.)

Results of surveys indicate that medical students and residents who were confident of their ability to screen for alcoholism and make treatment referrals were more likely to include screening and treatment in their clinical practice compared with peers with low confidence levels (Stokes et al. 1989).

According to student ratings at one university, teaching second-year medical students how to interview patients for the presence of alcohol and other substance abuse problems by using educational materials, simulated patient interviews, and instructor feedback has been successful (Spickard et al. 1989).

A decisionmaking system for primary care screening for heavy alcohol use and related disorders is presented in figure 1 (NIAAA 1987). The first step is to find out, in as unobtrusive a way as possible, whether the patient drinks. Patients who score below 2 on CAGE are asked about their drinking quantity and frequency through indirect, nonconfrontational questions.

General Hospitals

Diagnosis and referral of patients with alcohol use disorders should be facilitated in a general hospital for many reasons (Lewis and Gordon 1983). Patients hospitalized for alcohol-related conditions such as trauma and liver diseases may have difficulty denying the role of drinking and may be relatively receptive to offers of treatment.

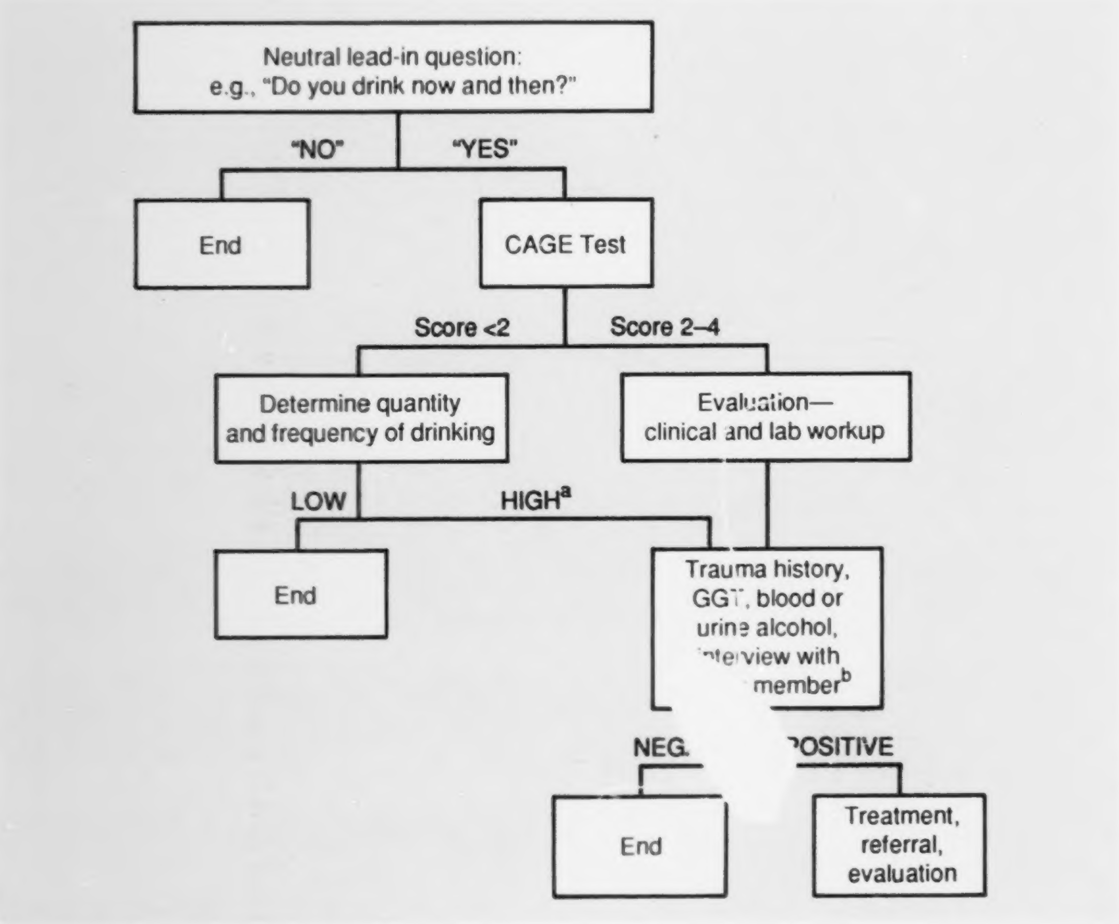
Neutral lead-in question:
e.g., "Do you drink now and then?"
"NO"
"YES"
End
CAGE Test
Score <2
Score 2–4
Determine quantity and frequency of drinking
Evaluation—clinical and lab workup
LOW
HIGH^a
End
Trauma history, GGT, blood or urine alcohol, interview with member^b
NEG.
POSITIVE
End
Treatment, referral, evaluation

FIGURE 1. Decision tree for primary care alcohol screening.

[a] High school consumption is defined as 60 to 80 g of absolute ethanol per day. (See Royal College of Psychiatry 1979 and Sanchez-Craig and Israel 1985.)

[b] Significant trauma history would be indicated by a score of 2 or higher on the five-item trauma scale designed by Israel and colleagues at the Addiction Research Foundation. The questions are asked in the following order: (1) Have you had any fractures or dislocations since you were 18? (2) Have you been injured in a traffic accident? (3) Have you had your head injured? (4) Have you been injured in an assault or fight? (5) Have you been injured after drinking?

SOURCE: Modified from NIAAA 1987.

Family and friends of these patients can assist in the diagnosis and encourage patients to seek treatment. The formal and informal linkages between the hospital and other health and human services can facilitate the referral process. Unfortunately, most general hospital staff seem to be unaware of their patients' alcohol-related problems, and diagnosis usually is not made until severe medical problems such as liver cirrhosis or pancreatitis emerge. The findings of two recent experimental investigations conducted in general hospitals in Scotland (Chick et al. 1985) and New Zealand (Elvy et al. 1988) demonstrate that general hospital programs can increase the proportion of patients with alcohol-related problems who are identified earlier, provided with intervention services, and referred to long-term care in the community when necessary. (See chapter X.)

Emergency Rooms

Alcohol plays a major role in trauma (Lowenfels and Miller 1984; Goodman et al. 1986; Haberman 1987). Waller (1988) estimated that 20 to 25 percent of all persons hospitalized with an injury have an identifiable alcohol use disorder. The high prevalence of injury among heavy drinkers suggests that a history of trauma may be useful in the early detection of alcohol use disorders (Abrams 1986; Clark et al. 1985; Maull et al. 1986; Skinner et al. 1984; NIAAA 1987).

Hospital emergency rooms, the point at which most trauma cases enter a hospital, may be appropriate sites for the screening and early detection of alcohol problems. Cherpitel (1988) studied emergency room admissions to a municipal general hospital and found that drinkers were more likely than abstainers to be admitted for injuries. Roizen (1988) reviewed emergency room studies and found alcohol use in 20 to 37 percent of all trauma cases.

Little has been published on the screening of emergency room patients for alcohol problems, probably because alcohol consumption surveys are too long to impose on a patient who has been injured or suddenly taken ill (Yates et al. 1987). Maull et al. (1984) even found that hospital entry due to injuries may decrease the likelihood that people with alcohol-related problems will be identified and linked to treatment through other channels. Patients who were admitted to a hospital for injuries received as a result of alcohol-impaired driving were found unlikely to be charged or convicted for driving while intoxicated even though a law enforcement officer strongly suspected alcohol involvement and positively assessed alcohol impairment.

There is strong support for routine blood alcohol testing as part of emergency room admissions (Maull et al. 1986; Soderstrom and Cowley 1987; Zuska 1981). Maull et al. (1986) maintained that physicians should assume alcohol involvement in injury cases until it is disproved by BAC measurement. Rockett and Putnam (1986) recommended that hospital staff record alcohol information routinely for trauma patients. Waller (1988) emphasized the need to search rigorously for signs of alcohol problems.

Despite the abundance of data linking alcohol and trauma, routine testing for alcohol in injury patients is uncommon (Maull et al. 1984; Simel and Feussner 1988). Chang and Astrachan (1988) found that hospital-based physicians tested only one-quarter of 320 motor vehicle accident patients in the emergency room of an urban hospital and did not refer for alcohol problem assessment or treatment any of the 47 patients who were BAC positive at 200 milligrams per deciliter or above. Soderstrom and Cowley (1987) surveyed U.S. trauma centers and found that only 55.2 percent conducted routine BAC testing.

Recognizing the crisis of trauma as a special opportunity for intervention, Gentilello et al. (1988) used a standard outpatient intervention technique (Social Network Intervention) to induce 17 inpatient alcoholic trauma patients at a level 1 trauma center to enter an alcohol treatment program. Patients were identified as alcoholics with data from family interviews and screening questionnaires. These authors emphasized that trauma surgeons are in a unique position to diagnose alcohol use disorders because they routinely determine BACs as the basis for assessing patients' physical and neuropsychological status and for planning surgical intervention. (See chapter X for a discussion of links between the screening process and interventions.)

Summary

Classifications of alcohol use disorders have evolved gradually; WHO and APA approaches have played dominant roles.

At present, diagnostic criteria in the revised version of the APA's DSM-III-R have been adopted worldwide by researchers and clinicians, and their inclusion in a future edition, DSM-IV, is under consideration. WHO's ICD-9, which introduced the concept of alcohol dependence syndrome, is undergoing review, and ICD-10 is being planned. Both DSM-III-R and the planned ICD-10 define alcohol dependence similarly and contain a category that allows classification of the medical and psychological consequences that are directly related to alcohol consumption and associated with a regular pattern of use. Both systems reflect a general evolution toward detailed assessment of alcohol use disorders using multiple diagnostic criteria.

Advances in assessment technology have led to the development of procedures for screening and diagnosis. Screening, an important preliminary step in the diagnosis of alcohol use disorders, is accomplished with questionnaires and interviews (often self-administered) for assessing psychosocial indicators of alcohol problems, and with laboratory tests and other biological measures for detecting biochemical markers of excessive drinking.

Key properties of screening instruments are validity (i.e., they measure what they are intended to measure), reliability (they measure consistently across time and raters), sensitivity (they accurately identify persons who have the target condition), and specificity (they correctly classify as negative those who do not have the condition). Because the balance between sensitivity and specificity is delicate, statistical techniques are used to select cutoff scores to classify subjects as positive or negative and to set the desired level of sensitivity and specificity in a given test.

The validity and reliability of self-report procedures (interviews, questionnaires, and computer-assisted tests) is a concern to professionals in the field. The computer-assisted assessment method has considerable potential. Patients have indicated preferring it over the self-administered questionnaire and the interview, and responses have been found to be reliable.

Researchers have had varying degrees of success with biochemical markers, which can be measured by laboratory tests. Some of these are blood levels of certain enzymes found in the liver and other organs, mean corpuscular volume (an index of red blood cell size), uric acid, blood lipids, and BAC.

A review of studies has shown that the MAST, SMAST, CAGE, and Reich screening instruments are clearly superior to biochemical markers in identifying known alcoholics, who may be less likely to misrepresent their drinking problems. Although questionnaires are more sensitive than biochemical tests in identifying these individuals, biochemical tests remain valuable for the use of hospital-based physicians in detecting hidden alcohol use disorders.

Although primary care physicians are in a key position to make early diagnoses of alcohol use disorders, they often misdiagnose or underdiagnose because of stereotypes regarding alcohol problems or inadequate training in this area. The coexistence of alcohol use disorders and psychiatric disorders (e.g., dementia in older people) also can complicate diagnosis. Greater emphasis on screening and treatment in medical education and training of residents could contribute significantly to early diagnosis and timely treatment referral.

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Chapter IX

Prevention

Introduction

Prevention efforts are aimed at reducing the adverse effects of single bouts of drinking as well as the social and medical problems that arise as a result of persistent high-risk drinking by alcohol abusers and alcohol-dependent persons. Prevention activities are undertaken by legislators, law enforcement officials, health professionals, educators, business leaders, and concerned citizens. In recent years, a public health approach to prevention has emerged. A key element of this approach is the recognition that reducing alcohol use problems requires strategies that affect the environment as well as individual behavior. Efforts aimed at the prevention of alcohol use problems employ a variety of methods, including public information and education, changes in the social contexts of drinking, and limitations on the availability of alcoholic beverages (Holder and Stoil 1988).

Prevention research also employs the public health model. In particular, the current emphasis is on studies concerning the host (i.e., the individual drinker) and the environment (i.e., the immediate drinking context). Two types of prevention research are conducted. Basic prevention research explores factors that influence the risk of developing alcohol use problems. These factors include individual characteristics that may place one at risk (e.g., age, gender, and family history), and factors within the environment that may affect risk (e.g., family interaction, workplace factors, characteristics of drinking establishments, and alcohol beverage prices). Applied prevention research evaluates the effectiveness of purposeful actions taken to reduce problems related to alcohol use. Such actions include measures to modify the drinking environment (e.g., legislation establishing minimum drinking age, laws regarding drinking and driving, and server training programs) and measures designed to change individual behavior (e.g., educational programs). Ideally, the findings of basic prevention research contribute to the development and implementation of prevention strategies.

This chapter summarizes basic prevention research on the contribution of certain environmental factors to the development of alcohol use problems and applied prevention research on the impact and outcomes of a variety of prevention initiatives. Research on individual characteristics that influence the risk of developing alcohol use problems is discussed in chapters II and III.

Basic Prevention Research

Research investigating the relationship between the price of alcoholic beverages and alcohol use problems such as motor vehicle crashes is one of the most promising areas of prevention research. The results of studies in this area suggest that an increase in Federal taxes equalizing the tax rate per ounce of alcohol indexed to inflation may lead to significant reductions in heavy drinking and in fatal crashes among youths.

A number of studies have also examined advertising of alcoholic beverages and other portrayals of alcohol in the media. Underlying such studies is the concern that these portrayals may contribute to alcohol use problems. Research in this area, however, has thus far yielded no conclusive evidence about the role of the media in alcohol use problems.

Recent research related to the price of alcoholic beverages and to alcohol portrayals in advertising and other media is reviewed in the following section. Recent studies in other basic prevention research areas also are highlighted.

Price of Alcoholic Beverages

Taxes imposed by Federal, State, and local governments affect the price of alcoholic beverages. Some evidence about the association between price and alcohol consumption comes from the results of natural experiments (e.g., comparisons of alcohol consumption in States with differing taxes on alcohol). Other information comes from econometric research, which uses available data to make projections about the possible impact of price changes on consumption and alcohol use problems through statistical modeling. Results of such research suggest that changes in price may affect both alcohol consumption patterns and alcohol-involved automobile crashes.

It is noted that stable Federal excise taxes combined with modest increases in State and local excise taxes have contributed to a decline in the real price of alcoholic beverages (Coate and Grossman 1987). The Federal tax on alcohol in beer and wine has remained constant since 1951, and the tax on alcohol in distilled spirits was increased in 1985 after remaining unchanged for nearly 35 years (Coate and Grossman 1987). Further, the Federal excise tax on alcohol in beer, the most popular beverage among youths who use alcohol, is one-third the tax on alcohol in distilled spirits (Coate and Grossman 1987). Between 1960 and 1980, the real price of beer fell by 27 percent; the real price of wine, by 20 percent; and the real price of spirits, by 48 percent (Cook 1981).

Econometric studies examined the effects of price on alcohol consumption and alcohol-involved automobile crashes. These studies used the existing prices of alcoholic beverages in the youths' places of residence as a base and derived estimates from available data on alcohol use among 16- to 21-year-olds in the United States between 1975 and 1981 (Grossman et al. 1987; Coate and Grossman 1988). Controlling for other variables that may be related to alcohol use and fatal motor vehicle accidents, such as age, sex, and family income, these studies have projected that higher real prices for beer would reduce the incidence of heavy drinking and frequent drinking among young people, as well as the number of young people who drink (Grossman et al. 1987; Coate and Grossman 1988).

This finding was not limited to youths who consume beer infrequently (less than once a week) or less heavily (one or two cans per typical drinking day); higher beer prices were also projected to have a significant effect on young people who drink frequently (1–7 times per week) and heavily (three or more cans of beer on a typical drinking day) (Coate and Grossman 1988). Using data from 1971–74, Grossman et al. (1987) estimated that even a small increase in the price of beer (10 cents per package of six 12-ounce cans) would reduce the number of 16- to 21-year-olds who drink by approximately 11 percent, the number who drink two or three times per week by 8 percent, and the number who consume three to five cans of beer on a typical drinking day by 15 percent.

In terms of fatal automobile crashes, Saffer and Grossman (1987a), combining Federal and State excise tax rates, have estimated that a 100 percent increase in the real beer tax (approximately $1.50 per 24-unit case of 12-ounce cans) would reduce highway mortality among 15- to 17-year-old drivers by about 18 percent; among 18- to 21-year-old drivers, by about 27 percent; and among 21- to 24-year-old drivers, by about 19 percent. Phelps (1988), using the data of Grossman et al. (1987) that combined autopsy data from national highway safety studies with data concerning the effects of price on specific drinking behaviors, projected that a tax amounting to approximately 35 percent of the retail price of beer would halve the number of alcohol-related fatalities among

16- to 21-year-old drivers. Phelps (1988) also estimated that a 50-percent tax would eliminate approximately 75 percent of these deaths.

The association between alcohol prices and youth fatalities in automobile crashes was further investigated by Saffer and Grossman (1987b); when other variables were held constant, States that had relatively high excise taxes on beer were found to have lower death rates in crashes for 15- to 24-year-olds. Saffer and Grossman (1987b) examined available data on variables such as motor vehicle death rates, real beer tax, and the number of young licensed drivers found in different States. They estimated that if tax had been indexed to the rate of inflation during 1975 through 1981, there would have been a 15 percent reduction in crash fatalities among 18- to 20-year-olds. These investigators also projected that by taxing beer as heavily as distilled spirits are taxed, such fatalities would have been decreased by 21 percent, and that such fatalities would have been reduced by 54 percent through a combination of these policies.

Higher prices for alcohol were also found to be related to lower rates of heavy drinking. Cook (1981) found that cirrhosis mortality, an indicator of 10 to 20 years of heavy drinking by individuals, was lower in 30 States that raised distilled spirits taxes, compared to States that did not raise taxes. Estimating from State-level mortality data in the same 30 States covering 1962–1977, Cook and Tauchen (1982) and Cook (1982) projected that an increase of $1 in State distilled spirits tax at that time would have reduced cirrhosis mortality by nearly 2 percent in a State, and that doubling the Federal distilled spirits tax would have reduced cirrhosis mortality by 20 percent in the Nation. These investigators also found that relatively small increases in the price of distilled spirits were associated with reduced death rates from automobile crashes (Cook 1981; Cook and Tauchen 1982).

Manning et al. (1989) recently estimated that current excise taxes on alcohol cover only about half the lifetime discounted costs that drinkers impose on others through collectively financed health insurance, pensions, disability, group life insurance, fines, motor vehicle accidents, and criminal justice costs. Specifically, they estimated that these "external costs" total $0.48 per ounce of alcohol consumed, approximately twice the current average (State plus Federal) excise and sales taxes on alcoholic beverages. These external costs are dominated by costs associated with alcohol-related traffic crashes.

Advertising and Other Media Portrayals of Alcohol

A persisting area of interest is the effect of advertising and other media portrayals on alcohol consumption and alcohol-related problems. Both the frequency and the content of these portrayals are of interest. An area of concern is that such portrayals may compete with and counteract the prevention messages transmitted in public education campaigns.

Impact of Advertising on Alcohol Consumption

Research has yet to document a strong relationship between alcohol advertising and alcohol consumption. In a recent review, Smart (1988) concluded from the available evidence that (1) advertising bans have had little impact on alcohol sales, (2) no consistent relationship exists between alcohol sales and restrictions or expenditures on advertising, and (3) the best designed experimental studies show no impact of advertising itself on alcohol consumption. Furthermore, methodologically sound studies that have examined the relationship between young people's day-to-day exposure to advertising and their consumption of alcohol have found the effect of advertising to be small compared to the impact of other variables such as peer associations (Smart 1988). However, other reviewers have differed in their conclusions. For example, a review by Atkin (1987) concluded that advertisements may stimulate alcohol consumption of adults and adolescents to at least a modest degree. Atkin also concluded that, although advertising appears to have a more limited effect on excessive, hazardous, and problematic drinking, it may be a significant contributing factor in creating or reinforcing these adverse alcohol use patterns.

Although single young males are more likely to report frequent heavy drinking and drinking-related problems (Hilton 1987), and drivers under the age of 21 have the highest rates of alcohol-involved fatal traffic crashes (Douglass 1982), little research has examined alcohol advertisements targeted specifically at college students (Breed et al. in press). Breed and his associates have examined alcohol advertising in college newspapers in 1977–78 (DeFoe and Breed 1979) and in 1984–85 (Breed et al. in press). Although the average number of inches of national alcohol advertising per college newspaper issue was lower in 1984-85 than in 1977–78, during both periods the amount of space devoted to alcohol advertising greatly exceeded advertising for books and soft drinks. In the 1977–78 period, 34.6 column inches per issue were devoted to alcohol advertising, compared to 1.4 for books and 1.2 for soft drinks (DeFoe and Breed 1979). During 1984–85, 23.8 inches were devoted to alcohol, 1.3 to books, and 0.5 to soft drinks (Breed et al. in press).

At the time of the 1984–85 study, not all States had raised their minimum drinking age for alcoholic beverages to 21. However, extensive alcohol advertising was found even at colleges in States where the minimum drinking age was 21. There were no significant differences in total column inches devoted to alcohol advertising between the States with a drinking age of 21 and those with a lower minimum (Breed et al. in press). Furthermore, in 1984–85, when space devoted to national alcohol advertising was compared with all national advertising, a greater proportion of national advertising was given to alcohol advertising in schools with lower male enrollments. The investigators suggested that this finding provides evidence that national alcohol advertisements may be targeting schools with greater female enrollment (Breed et al. in press).

Although a number of experimental studies have examined the short-term effects of alcohol advertisements (Ackoff and Emshoff 1975; Brown 1978; McCarty and Ewing 1983; Kohn et al. 1984; Kohn and Smart 1984, 1987), Smart (1988) noted that none were ideal methodologically, some used artificial and contrived experimental drinking situations, and the attempts of most to mislead subjects about the purpose of the research may have affected study results. A laboratory study by Kohn and Smart (1987) supports the latter possibility. Researchers found that the group of women who saw nine wine commercials during videotaped television programs drank more wine than the group who saw three commercials, and the consumption of women who saw no commercials was midway between the other two groups. Subjects' responses to a debriefing questionnaire assessing suspiciousness about the study indicated that some subjects were suspicious of study objectives, although their specific suspicions were generally incorrect. The suspicious women appeared to resist drinking in the moderately persuasive condition (three commercials); their responses therefore reduced the average consumption of the total group of subjects in that condition. However, the suspicious women appeared to yield in the more intensive condition (nine commercials). These results suggest that personality factors such as suspiciousness and persuasibility should be taken into account in designing and analyzing the results of laboratory studies on the effects of advertising on alcohol consumption (Smart 1988).

Holder (1988) discussed the difficulty of demonstrating that alcohol advertising, by itself, causes alcohol problems and noted that advertisements are part of a complex interaction of real-world factors leading to alcohol-related problems that is unlikely to be replicated in a laboratory (Holder 1988). However, Smart (1988) suggested that, with better designs and procedures, experimental studies are most likely to answer questions about the effects of advertising.

Reviewers have also differed in their conclusions about available data: While Atkin (1988, cited in Atkin 1989) has interpreted study findings in this area (Brown 1978; McCarty and Ewing 1983; Kohn et al. 1984; Kohn and Smart 1984, 1987; Sobell et al. 1986) as suggesting limited effects of advertising on consumption, Smart (1988) has noted that the best controlled laboratory studies (e.g., Kohn and Smart 1984, 1987; Sobell et al. 1986) showed no overall effect of alcohol advertising on alcohol consumption. Although there is disagreement about the potential utility of laboratory research in studying advertising effects as well as about interpretations of available experimental data, it is clear that further research is required to understand the role that advertising may play in alcohol consumption.

Alcohol on Television

Reducing the use and glamorization of alcohol in the mass media or at least emphasizing the realistic portrayal of the negative consequences of consumption is believed to be a useful prevention measure (Breed et al. 1984). It is assumed that frequent drinking scenes on television help to create social expectations and norms that drinking is expected and appropriate in all situations, thereby increasing both consumption and mistaken beliefs about alcohol and its consequences.

Laboratory research directly studying the relationship between portrayals of alcohol on television and alcohol consumption has been limited. The results of two studies suggest that television may influence young children's beliefs about alcohol. Rychtarick et al. (1983) examined this relationship indirectly in a laboratory study demonstrating that children aged 8 to 11 who viewed a popular television show with drinking

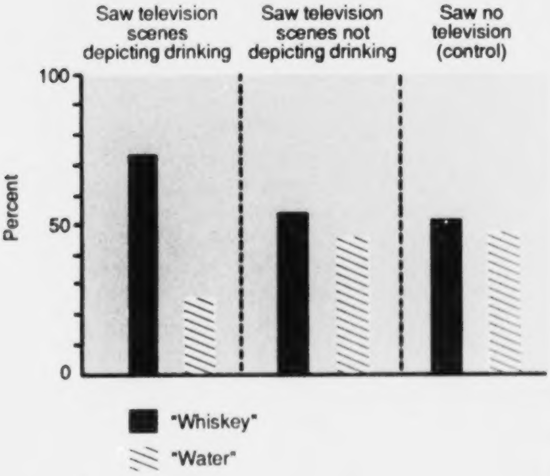


FIGURE 1. Percentage of children who chose "whiskey" or "water" as appropriate beverage to serve adults after viewing televised scenes depicting and not depicting drinking.
SOURCE: Rychtarik et al. 1983. Copyright 1983 by Pergamon Press.

scenes were more likely to name alcohol than water as an appropriate beverage to serve adults than were children who viewed the same show with the drinking scenes deleted (see fig. 1). An experimental study of fifth- and sixth-grade children (Kotch et al. 1986) found that boys (but not girls) who saw a videotaped television show including drinking scenes were significantly more likely to indicate that the "good things" about alcohol were more important than the "bad things," than were boys who saw the videotape without drinking scenes. However, a laboratory study by Sobell et al. (1986) found no effect of televised drinking scenes or advertising on alcohol consumption by male college students whose drinking involved using alcohol at least once a month, with beer accounting for at least 20 percent of their total alcohol intake.

In content analyses of television programs extending back to the mid-1970s, alcohol has been found to be the most common drug used on U.S. television, as well as the most frequently used beverage (Wallack et al. 1987). Breed et al. (1984) found that the number of acts of drinking occurring in television programs rose from slightly fewer than five per hour during the 1976–77 season to more than eight per hour in 1981–82. Drinking acts included people actually consuming alcohol or preparing to drink (ordering, pouring, accepting, or holding a drink or having one nearby). In the 1984–85 television season, an average of 10.5 acts of drinking occurred per hour (Wallack et al. 1987). Whereas alcohol accounts for only 16 percent of total beverage use in the "real world" (U.S. liquid...1984, cited by Wallack et al. 1987), alcohol accounted for 74 percent of the beverages seen on television during the 1984–85 season.

In the 1984–85 season, only about 1 percent of the scenes in which alcohol appeared involved heavy drinking and its consequences. Rather, most were classified as "alcohol-incidental" scenes that included sipping, bottles or glasses on a wet bar, signs reading "cocktails," or passing references to alcohol. Furthermore, images of people preparing to drink were shown three times more frequently than people actually drinking. According to Wallack et al. (1987), these findings suggest that alcohol is treated "almost as a neutral substance, almost as a prop" on television.

Similar findings were also recently reported by Hansen (1986), who analyzed the portrayal of alcohol during 2 weeks of prime-time television programs in Great Britain during 1983. Visual and verbal references to alcohol appeared in approximately two-thirds of all programs, but actual consumption occurred on only one-third of the programs in which alcohol appeared. Three-quarters of the drinking characters were portrayed as belonging to the middle or upper middle class and only one-quarter as working class. Although about 60 percent of the drinking characters consumed alcohol in ordinary settings, one-third were shown drinking in luxurious surroundings, and only 5 percent in a poor or destitute environment.

Taken together, these content analyses of television shows in the United States (Wallack et al. 1987) and Great Britain (Hansen 1986) provide support for the assertion that alcohol is ubiquitous and taken for granted on television and that drinkers portrayed on television are frequently glamorous (Wallack et al. 1987). However, although these analyses document an unbalanced portrayal of alcohol use on television, there is little conclusive evidence that television's portrayal of alcohol affects viewers' actual consumption of alcoholic beverages.

Environmental Risk

An understanding of characteristics of environments that promote or reduce alcohol consumption and alcohol use problems is relevant to the development of effective prevention measures to modify environmental risk.

Family

The influence of the family environment has been investigated in terms of factors that may contribute to later alcohol problems. In particular, the relative roles of genetics and environment in the development of alcohol dependence have been an area of considerable research interest (see chapter III for a discussion of research on this topic). Research has also related family variables to the initiation of drinking by young people. Research has found that most teenagers are introduced to alcohol at home in the presence of their parents (Davies and Stacey 1972; Maddox and McCall 1964); both abstinence and drinking in parents are frequently paralleled by abstinence or drinking by their adolescent children (Harford 1984). In addition, family interaction has been studied in families with an alcohol-dependent member (see chapter VII for a discussion of these family interaction studies). The findings of a recent study that observed couples with an alcohol-dependent member (Leonard and Jacob 1988) suggested that the occurrence of negative behavior during a specific drinking session is associated with the dependent drinkers' general drinking patterns (that is, whether they are episodic or steady drinkers). The dynamics of drinking in a family were also examined in a recent study by Corbett et al. (in press) investigating drinking patterns and drinking-related problems of Mexican-American husbands and wives. Drinking patterns, problems, and expectancies were found to differ between husbands and wives, but spouses' drinking levels were correlated; that is, husbands who were heavy drinkers tended to have drinking rather than abstaining wives (Corbett et al. in press).

Workplace

Although intervention programs have been established in many companies to assist individuals who have begun to develop alcohol use problems (see chapter X for a discussion of employee assistance programs), little research has been conducted to assess the role of the work environment itself in promoting or reducing alcohol-related problems. In a recent review of the history and effects of drinking policies in the American workplace, Ames (1989) noted that employee assistance programs, rather than enforcement of company rules and regulations about alcohol use during working hours, are the dominant alcohol policy. Ames and Janes (1987) investigated a heavy-drinking subculture in a blue-collar work environment. Although workplace characteristics such as the importance of drinking in work-related social contexts and the permissiveness of the work environment played a major role in promoting heavy alcohol consumption, the social and cultural backgrounds of workers also were determining factors (Ames and Janes 1987). Based on study findings, the authors made recommendations for environmental changes that addressed both worksite factors and worker characteristics related to heavy alcohol consumption. Recommendations included providing free hot lunches inside the plant to inhibit lunch hour and parking lot drinking and organizing groups to promote leisure activities appropriate to workers' interests and economic abilities.

Drinking Establishments

Although research indicates that a majority of people who are arrested for driving while intoxicated (DWI) are coming from licensed drinking establishments, particularly bars (O'Donnell 1985), the contribution of characteristics of drinking sites to alcohol use problems is not well documented or understood (Holder 1988). A recent review of available research (Single 1987) suggests that the consumption rate of drinking confederates affects individual rates of consumption and that factors such as the floor plan of bars and the size of drinking groups influence the duration of stay and, consequently, the amount of alcohol consumed.

Individual Risk Characteristics

Knowledge and understanding of alcohol epidemiology are relevant to developing successful prevention measures. Epidemiological research has examined a variety of individual characteristics—including age, gender, and race and ethnicity—that are related to alcohol consumption and risk for alcohol problems. For example, both alcohol abuse and alcohol dependence are more likely to occur among men than among women; young, single men are more likely to be frequent heavy drinkers and to report alcohol dependence and alcohol-related problems (Hilton 1987). Black men and white men have similar drinking patterns overall, although black men had somewhat higher abstention rates than whites (29 percent versus 23 percent) and white men were somewhat more likely to be heavier drinkers (Caetano 1989; Herd 1988b, 1989). However, black men appear to experience some types of alcohol-related problems at lower levels of consumption (Herd 1988a). Hispanic men (Caetano 1986) and American Indians also have high levels of alcohol use problems; however, the degree of problems varies among different subpopulations of these groups. (See chapter II for further discussion of this and other research on individual risk characteristics.)

Research also has examined early behavioral characteristics of children that predict use of alcohol and other drugs in adolescence. Kellam and his associates (1983) found that shyness among first-grade boys (but not girls) was associated with less alcohol and other drug use when these children reached age 16 or 17, whereas aggressiveness in first grade was associated with increased alcohol and other drug use by boys (but not by girls).

Also relevant to the topic of individual risk is the topic of fetal alcohol syndrome (FAS). Understanding of the characteristics of women at risk for bearing a child with FAS is essential to planning programs to prevent this problem. (See chapter VI.)

Individual-Environment Interaction

The interaction of the individual and the environment is also a concern of basic research related to prevention. Relevant topics include the involvement of alcohol in accidents and trauma, the role of alcohol in crime and violence, and adolescent risk factors.

Accidents and Trauma

Research to measure and understand alcohol's role in accidents and trauma is essential for planning prevention programs and providing a baseline for evaluation. The role of alcohol in motor vehicle crashes has been studied extensively. Research findings indicating the overrepresentation of young people in alcohol-related crashes and increases in such crashes that occurred after the legal minimum drinking age for alcoholic beverages was lowered in the early 1970s (Vingilis and DeGenova 1984) led to Federal incentives for the States to increase the minimum drinking age. Alcohol's role in other types of accidents has been researched less extensively, but alcohol has been implicated in fires and burns and falls (Howland and Hingson 1988). Research also has suggested that the severity of trauma is increased for intoxicated victims (Roizen 1988) (see chapter VII for further discussion of the role of alcohol in accidents and trauma).

Crime and Violence

The role of alcohol in crime and violence, including family violence, continues to be an area of concern and basic prevention research. Methodological problems are pervasive in these research areas, and few data from methodologically sound studies are available to allow firm conclusions about alcohol's role or to assist in the development of effective prevention programs. (See chapter VII.) Laboratory research on alcohol and aggression in humans and animals allows the controlled study of relevant behaviors and should further the understanding and the development of strategies to prevent violent alcohol-related behavior. (See chapter IV.)

Adolescent Environmental Risk Factors

The role of peers is an important environmental risk factor related to adolescent drinking. Research (Jessor et al. 1972) has found that perceived peer support for drinking was the most important variable accounting for the initiation of drinking by previously abstaining high school students. Grube and his associates (1989) also found that perceived peer drinking was the primary predictor of current alcohol use by adolescents in Ireland. Recent prevention efforts, discussed elsewhere in this chapter, that have targeted young people have emphasized the role of peers in alcohol and other drug use.

Problem behaviors such as use of alcohol and other drugs, smoking, delinquency, and precocious sexual intercourse have often been found to occur together in the same adolescent in research conducted in the United States (Jessor and Jessor 1977; Donovan and Jessor 1985; Donovan et al. 1988). Unconventionality in both social environment and personality has been postulated to be the underlying cause of this syndrome of problem behavior (Jessor and Jessor 1977). Research recently reported by Grube et al. (1989) indicated that smoking and involvement with other problem behaviors were also associated with current drinking among adolescents in Ireland. A need to develop prevention and early intervention efforts designed to address the factors underlying such clusters of risky behaviors has been noted (Douglass 1982; Bradstock et al. 1987; Grube et al. 1989). Chapter X discusses these behaviors as they relate to drinking and driving among adolescents.

Applied Prevention Research

Applied research in prevention has evaluated the impact of measures taken to modify the environment and approaches designed to change individual behaviors.

Measures to Change the Environment

Much of the research on environmental strategies has examined policy measures related to alcohol, such as legislation on the minimum drinking age and laws concerning drinking and driving. Other environmental measures studied include changes in the actual context of drinking such as those brought about by server training, transportation alternatives for drinking drivers, and modifications in the design of vehicles and roadways to prevent alcohol-related crashes.

Minimum Drinking Age

In the early 1970s, many States reduced the legal minimum drinking age for alcoholic beverages, usually from 21 to 18. This reduction was followed by increases in alcohol consumption and alcohol-related accidents among drivers aged 18 to 20 (Vingilis and DeGenova 1984). Most of these States increased the legal drinking age by early 1984, although not all of them increased it to 21 (Bonnie 1985). Because increasing the legal drinking age to 21 was viewed as a prevention strategy, incentive to achieve a standard minimum drinking age of 21 was provided in July 1984 by legislation cutting off Federal highway funds from States that did not comply by certain dates. Any funds withheld were to be returned to a State when it enforced this minimum drinking age. All States and the District of Columbia had complied with the legislation by 1988.

Impact on Traffic Crashes. Data from the Fatal Accident Reporting System (FARS) of the National Highway Traffic Safety Administration (NHTSA) demonstrate that the greatest reduction in fatal traffic accidents involving drunk drivers from 1982 to 1986 was among drivers aged 16 to 20 in States that increased their minimum drinking age to 21 (NHTSA 1988a). This group showed a 30-percent reduction in fatal crashes involving intoxicated drivers during this period (see table 1).

The U.S. General Accounting Office (GAO) recently synthesized the results of 14 studies that were selected on the basis of quality of data, design, and methodology from among 49 studies that evaluated the effects of laws raising the legal drinking age (GAO 1987). The GAO study found that although the individual evaluations differed in study location, design, analysis method, and outcome measure, the direction and often the size of effects attributable to an increase in drinking age were generally similar. Reductions were found in traffic crashes among the age group directly affected by the increase in minimum drinking age in almost every State that was evaluated (GAO 1987). However, the GAO report also indicated that little evidence is available to suggest that an increase in minimum drinking age affects the involvement of 16- and 17-year-old drivers in alcohol-related accidents as it does for drivers 18-20 years old.

Most studies examining the impact of minimum-drinking-age legislation on traffic accidents are based on the premise that the combination of age, driving, and alcohol is responsible for the increased risk among young drivers for alcohol-related crashes (Asch and Levy 1987). However, it has also been suggested that inexperience in drinking may create a traffic fatality hazard independent of age (Males 1986; Asch and Levy 1987). Based on a cross-sectional analysis of traffic fatalities in the 50 States during 1978, Asch and Levy (1987) found no relationship between the legal drinking age (which at that time ranged from 18 to 21) and fatality rates. However, they found that youths in the first year of drinking experience had a 10- to 20-percent greater risk for fatalities in general, and for single-vehicle fatalities in particular (Asch and Levy 1987).

If experience in drinking independent of age is associated with risk for traffic fatalities, increasing the minimum legal drinking age may serve mainly to shift the age distribution of traffic fatalities (Asch and Levy 1987). Thus an increase in the legal drinking age may be followed at first by a reduction in fatalities in the age group directly affected by the change, but this reduction would eventually be offset by an increase in fatalities as this group reaches the legal drinking age (Asch and Levy 1987).

There is recent evidence that changes in the legal drinking age have had a long-term impact on fatalities. DuMouchel et al. (1987) found an average 13 percent decrease in fatal nighttime accidents involving 18- and 19-year-old drivers in a study of 26 States that raised the minimum

TABLE 1. Reduction in drivers with BACs of 0.10 percent or higher for groups of States with various minimum legal drinking ages, by age group, 1982 versus 1986

		Percent		
Age group	**Drinking age**	**1982**	**1986**	**Reduction**
16 to 20	Always 21[a]	30.6	23.8	22
	Never 21[b]	33.2	26.9	19
	Changed to 21[c]	29.8	21.0	30
21 to 44	Always 21	40.3	36.9	8
	Never 21	43.9	40.3	8
	Changed to 21	36.3	32.1	12
45 and over	Always 21	28.1	24.0	15
	Never 21	30.4	27.0	11
	Changed to 21	24.6	22.0	11

[a] Arkansas, California, Illinois, Indiana, Kentucky, Michigan, Missouri, Minnesota, Nevada, North Dakota, Oregon, Pennsylvania, Utah, Washington, Wyoming.

[b] Colorado, District of Columbia, Hawaii, Idaho, Iowa, Louisiana, Minnesota, Montana, North Carolina, Ohio, South Carolina, South Dakota, Texas, Vermont, West Virginia, Wisconsin.

[c] Alabama, Alaska, Arkansas, Connecticut, Delaware, Florida, Georgia, Kansas, Maine, Maryland, Massachusetts, Mississippi, Nebraska, New Hampshire, New Jersey, New York, Oklahoma, Rhode Island, Tennessee, Virginia.

SOURCE: NHTSA 1988a.

drinking age between 1975 and 1984. Followups 1 and 3 years after drinking-age changes went into effect found that the decreased rate was maintained. A 16-percent decrease in injury-producing single-vehicle nighttime crashes among young drivers also was maintained in a 6-year followup study of fatalities in Michigan after an increase in the minimum drinking age (Wagenaar 1986).

Impact on Alcohol Consumption. The primary intent of increasing the minimum drinking age is to reduce adolescents' access to alcohol and thereby to reduce drinking and its harmful consequences in this age group (Williams 1986). GAO's review concluded that among those affected by the change, available evidence "supports the claim that raising the purchase age reduces both the consumption of alcohol and the incidence of driving after drinking" (GAO 1987, p. 3) but noted that the results of reviewed studies cannot be generalized to specific States or jurisdictions, because most of the available data pertains to New York State and the research is sparse. Available evidence on alcohol consumption and drinking and driving among 16- and 17-year-olds is insufficient to determine the effects of legislation on those youths younger than the minimum drinking age since study results are mixed (GAO 1987).

Although changes in the laws regulating minimum drinking age may have had some effect on consumption, they have not eliminated access to alcohol nor deterred many adolescents from drinking (Donovan in press). During the period in which the laws were changed, there was a decline in the proportion of university students who drank, but the proportion of students who were heavy drinkers (those who consumed six or more drinks at any one sitting more than once a week) remained constant (Engs and Hanson 1988). Mayhew et al. (1986) noted that it will be important to determine how changes in these laws affect both the quantity and the frequency of consumption by young people; if these two aspects of drinking behavior are affected differently by changes in the legal minimum drinking age, the implications for driving after drinking would also be different.

Other Changes in Availability

Laws and regulations determining the number and types of outlets that may sell alcoholic beverages and the hours during which alcohol may be sold also influence alcohol consumption and related problems. A study using county-level data from Ontario, Canada, found a positive association between retail availability of alcohol, alcohol consumption, and alcohol-related morbidity and mortality (Rush et al. 1986). Recent research results suggest that communities use certain local ordinances restricting availability to prevent problems related to alcohol. Other research findings have documented types of changes in the regulation of alcohol sales that may increase such problems.

A natural experiment (Blose and Holder 1987a,b; Holder and Blose 1987) examining the effects of changes in availability of distilled spirits was made possible by the implementation of laws in North Carolina in 1978 that permitted the sale of liquor by the drink at licensed clubs and restaurants; previously patrons could bring distilled spirits to these establishments and purchase ice and "setups." Comparisons of North Carolina counties where sale of liquor by the drink was legal but had not been implemented indicated that availability of liquor by the drink resulted in a 250-percent increase in the number of establishments where liquor could be purchased (Blose and Holder 1987b). Increases in distilled spirits sales ranged from 6 percent to 7.4 percent in the counties implementing liquor by the drink (Holder and Blose 1987), and increases in alcohol-related traffic accidents in these counties ranged from 16 percent to 24 percent (Blose and Holder 1987a).

Wittman and Hilton (1987) examined the use of planning and zoning ordinances to regulate alcohol outlets in California cities. Cities can issue or deny conditional use permits after a review process to determine if the proposed land use could do harm. Conditional use permits can specify restrictions on hours, decor, or serving practices in businesses planning to serve alcohol (Wittman 1986). The study found that about two-thirds of California cities that issue conditional use permits used them in local zoning activities to regulate at least one type of alcohol outlet (bar, restaurant, liquor store, grocery store, or convenience store). About half of these cities required conditional use permits for all outlets selling alcoholic beverages for onsite consumption as well as for at least one type of outlet selling for offsite consumption; the remainder required permits for varying types of onsite establishments. Cities that used permits for both onsite and offsite establishments perceived more problems connected with alcohol outlets than cities that applied permits only to onsite establishments. The authors interpreted these findings as suggesting that cities are willing to use local ordinances to prevent alcohol problems and that they do so in a selected and graduated manner, depending on the perceived severity of outlet-associated problems (Wittman and Hilton 1987).

A current debate in several States concerns whether gasoline stations and convenience stores that sell gasoline should be allowed to sell alcoholic beverages (Wagenaar and Farrell 1989). For example, the emergence of a new type of retail sales outlet for beer and wine—the gas station minimart—has been an issue in California (Ryan and Segars 1987). The controversy centers on concern raised by public officials, law enforcement officers, and planners that the increase in outlets like minimarts not only increases the availability of alcohol but may also increase rates of drinking and driving and may link motor vehicle products to alcoholic beverages. Furthermore, there was also concern that, because minimart employees are often young people, higher rates of illegal sales of alcoholic beverages to underage persons may occur.

A study conducted in Orange County, California, found that 85 percent of persons who purchased alcoholic beverages and gasoline at the same outlet consumed the beverage in their cars (California Council on Alcohol Problems 1986, cited by Ryan and Segars 1987). Research in San Diego County (Ryan and Segars 1987) found that alcoholic beverages purchased in liquor stores, convenience stores, and gas station minimarts were equally likely to be consumed in a car. Alcoholic beverages purchased in supermarkets were less likely to be consumed in a car, presumably because such purchases are planned for at-home consumption or storage (Ryan and Segars 1987). However, although gas station minimarts represented 6 percent of the total alcohol outlets in San Diego County, they were responsible for 15 percent of reported purchases of alcoholic beverages and 17 percent of reported occurrences of drinking in a car (see table 2).

Recent research has also examined the relationship between traffic crashes and an increase in the number of outlets selling alcoholic beverages for onsite consumption. Smith (1987) examined the consequences of introducing Sunday sales of alcohol in hotels in New South Wales, Australia; before the introduction of sales at hotels, alcohol had been available on Sundays only at clubs. In the 2 years after the introduction of Sunday sales by hotels, there were 20 percent more fatal crashes between noon and midnight than in the 2 previous years (Smith 1987).

Research conducted in Australia also found that the days of the week and the hours of the day when alcoholic beverages are available for purchase may influence the timing of traffic crashes. In Tasmania, Smith (1988) studied the effect of introducing flexible trading hours that allowed hotels to determine the number and schedule of hours that they would remain open. Although the total hours that hotels stayed open daily remained approximately the same in the

TABLE 2. Consumption of alcoholic beverages in cars by type of sales outlet, San Diego County, 1985

Type of outlet	Estimated number of outlets[a]	Percent of total outlets	Percent of reported purchases	Percent of occurrences of drinking in car
Liquor store	432	25	42	43
Convenience store	812	47	26	28
Supermarket	379	22	17	12
Gas station minimart	104	6	15	17
Total	1,727	100	100	100

[a] Based on percentage from city sample used on known county total outlets. Survey results indicate 3 percent of total outlets were minimarts as of June 1984. For estimation purposes, total percentage for minimarts was doubled to 6 percent in recognition of increases in such outlets. Convenience stores were reduced by 3 percent.

SOURCE: Ryan and Segars 1987.

year after the introduction of flexible trading hours, the hotels closed later, presumably because of increased patronage at later hours. The number of accidents between 10 p.m. and 6 a.m. increased by 10 percent compared to the preceding 5 years.

A review of relevant research on drivers who were arrested for DWI or found impaired during roadside surveys suggested that approximately half of drinking drivers are coming from onsite-consumption establishments, particularly bars, although only about a quarter of all alcohol is sold at such establishments (O'Donnell 1985). Price incentives such as happy hours promoted by drinking establishments may be viewed as one element of alcohol availability (Holder 1988). However, research findings related to this possibility are inconclusive. An observational study conducted before and after a ban on happy hours found no significant change in alcohol consumption or sales to patrons of five bars in metropolitan Toronto during a 4-week period after the ban was initiated (Smart and Adlaf 1986). In contrast, in an earlier experimental study of price promotion conducted in a controlled setting, Babor et al. (1978) found that, during periods of reduced prices, both moderate- and heavy-drinking subjects (single men who were students or temporarily unemployed) increased their consumption of alcohol; the increase was not accompanied by decreases in consumption at other times of the day. Babor and his associates (1980) also found that happy hour promotions increased consumption among a selected group of patrons of a bar in the Boston area (the individuals were selected because they had been observed to be regular patrons). Further research will be required to determine if the impact of happy hours varies according to drinker characteristics as suggested by this group of studies.

Drinking-and-Driving Laws

A primary objective of drinking-and-driving laws is general deterrence. This model of prevention is based on the assumption that the threat of sanctions such as fines, imprisonment, or license revocation will prevent individuals from engaging in a specific behavior (Donovan in press).

Ross (1985) reviewed evaluations of a variety of deterrence programs, including enforcement crackdowns, sobriety checkpoints, mandatory jail, complex "tough" laws that emphasize increased severity of punishment as well as increased certainty of punishment, and swift punishment through administrative license suspension. He concluded that deterrent strategies that increased perceived certainty of punishment had short-term effectiveness, but strategies that increased severity or swiftness of punishment had not been found to be effective. Furthermore, severe punishment produced unexpected and unwanted perturbations in the criminal justice system, including delay, postponement, and even avoidance of punishment (Ross 1985).

However, there is accumulating evidence that problems in enforcing deterrence measures as well as in the scope and duration of such efforts may have influenced the outcomes of some deterrence programs. For example, research findings have suggested that the perceptions, attitudes, and priorities of police officers and administrators may affect the success of a deterrence strategy. In a survey of administrators and uniformed officers in the Province of Ontario, Vingilis et al. (1986) found that the estimated number of arrests per officer for impaired driving was 10 per year. Yet, an evening roadside survey (Interministerial Committee on Drinking Driving 1980, cited in Vingilis et al. 1986) indicated that 6.6 percent of the drivers stopped were impaired. Insufficient personnel and problems such as slow court processing, inadequate sentencing, and lenient attitudes of judges and prosecutors were among the problems that uniformed officers and administrators reported as most important in limiting their enforcement of drinking-and-driving laws. The results of this survey were similar to findings reported in earlier surveys conducted in New Zealand (Hurst 1980) and to findings in a survey of Alcohol Safety Action Project officers (Young and Co. 1974).

In the Ontario survey (Vingilis et al. 1986), 59 percent of the officers believed that the public's attitude toward drinking and driving was characterized by apathy and lack of support for enforcement: The public was unconcerned, unaware of the seriousness of the problem, sympathetic with drivers who get caught, and convinced that police had more important things to do. Both uniformed police and administrators gave drinking-and-driving enforcement a mid-range priority when ranking the amount of police time that should be accorded to various offenses. Vingilis et al. (1986) suggested that such perceptions reduce the motivation of law enforcement officers to arrest alcohol-impaired drivers.

Problems in enforcement were also reported in a study of the impact of administrative license revocation (Ross 1987a). Under administrative license revocation, which has been enacted in a number of States, the offender's driver's license is taken by the arresting police officer if the offender's blood alcohol concentration (BAC) is 0.10 percent or more or if the offender refuses a BAC test (Waller 1985). The driver receives a temporary permit to drive for a few days and may request judicial review after the license revocation has gone into effect. The prediction of a deterrent effect for license revocation is related to "theoretical and common sense expectations for this countermeasure, which can be viewed as likely to increase the certainty as well as swiftness of punishment" (Ross 1985, p. 126).

Ross (1987a) reported promising results in an evaluation of an administrative license-revocation program in New Mexico. A reduction of approximately 10 percent in the proportion of crash-related fatalities involving alcohol-impaired drivers or pedestrians was maintained for 20 months after the law was passed. Ross noted that the program's success was achieved despite police and judicial resistance to the law that apparently reduced the actual risk of punishment for drunk drivers (e.g., the average number of DWI arrests declined by 18 percent in one New Mexico city and 54 percent in another). Further, although the program increased actual swiftness of punishment, lagging media interest limited communication of this fact, and there also was evidence that the public frequently ignored or misunderstood the law.

Similar findings were reported by Vingilis et al. (1988), who examined the deterrent impact of Ontario's 12-hour license suspension law and the process by which the law was enforced. This law gives the Ontario police the authority to conduct random spot checks to detect drinking drivers and to suspend for 12 hours the licenses of drivers showing a BAC of 0.05 percent or more on a roadside screening device or evidentiary breath tester. Because the law allowed immediate punishment for drinking and driving without a time-consuming arrest process, police resistance to implementing the law was expected to be reduced, and it was hypothesized that more drinking drivers would be stopped by police.

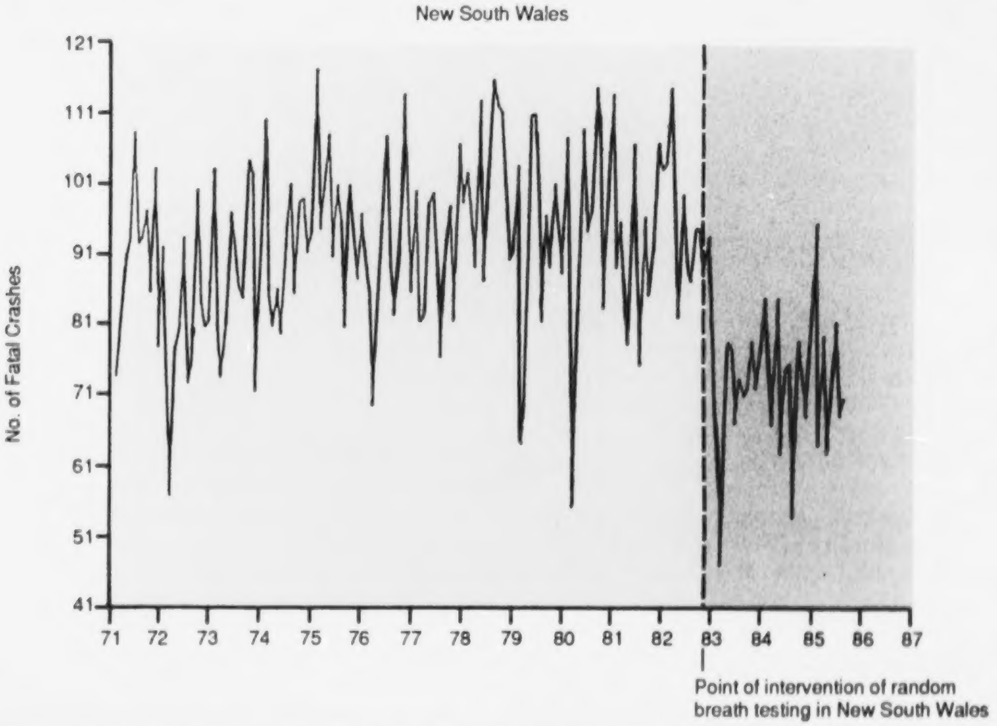
An evaluation of the law's deterrent impact suggested that the law may have had a relatively limited short-term effect on the proportion of alcohol-related fatalities. However, a process evaluation indicated that there was no organized media campaign about the law, that media coverage of the new law was sporadic and short-lived, that the public's awareness of the law was generally limited, and that specific knowledge was low. Further, 6 months after enactment, 41 percent of the police forces surveyed reported that they did not own the screening devices necessary to enforce the law. The authors suggested that the limited impact of the new law was likely to have been due to lack of publicity and enforcement (Vingilis et al. 1988).

The relatively short-term effects of deterrence programs implemented in France and the United Kingdom also seem to be related to the manner in which the deterrent approach was implemented. In a program demonstrating a short-term effect in the United Kingdom (Ross 1973, 1984), police officers could test the breath of any driver involved in an accident or traffic law violation. About half of the tests administered yielded BACs of 0.08 percent and above. Because other research has indicated that random tests of drivers would be expected to find BACs of 0.08 percent or higher in less than 1 percent of all drivers (Borkenstein et al. 1964, cited by Ross 1973), these findings suggest that police may have been selective in choosing individuals for testing and, for example, testing only when there were overt signs of intoxication (Ross 1973). In a French program also having a short-term impact (Ross 1984), police were to test the breath of all drivers who passed through roadside checkpoints. Only about 0.4 percent of the tests were recorded as positive during a 6-month period, less than one-fourth of the percentage of positive tests recorded in an independent roadside survey conducted in France during the same period. This result has been attributed to "official diffidence in enforcing the legislation" (Ross 1984).

The results of these studies are consistent in documenting inadequacies in the enforcement of deterrence programs. In light of the problems in the enforcement of these programs, short-term but positive effects of deterrent measures can be viewed as promising findings that call for improved implementation of deterrent interventions and further research into their long-term impact.

The results of a random breath-testing program recently investigated in Australia (Homel 1986) suggest that the nature of enforcement efforts can influence the duration of their effects. The long-term impact of this program compared to the programs in the United Kingdom and France was attributed to a substantial expenditure to publicize the program and to the sheer scope of the law enforcement effort, which, during its first year, resulted in testing approximately one of every three licensed drivers in New South Wales (Homel 1986). For 32 months after the program was implemented, monthly fatalities were reduced an average of 23 percent compared to the previous 6 years (see fig. 2).

The timing and duration of enforcement may also have some influence on the effectiveness of police "blitzes," i.e., efforts by local jurisdictions to increase the probability that alcohol-impaired driving will be detected and cited (National Research Council 1987). Although early research on these efforts generally yielded a transient effect



Point of intervention of random breath testing in New South Wales

FIGURE 2. Monthly fatal crashes in New South Wales, January 1971 to July 1985.
SOURCE: Homel 1986.

similar to other deterrent efforts, the blitzes studied were short (National Research Council 1987). More extended efforts were recently investigated in Stockton, California (Voas and Hause 1987), and Charlottesville, Virginia (Voas et al. 1985, cited by National Research Council 1987). In Stockton, a 3-month blitz was conducted from October through December each year for 3 years. The blitzes tripled arrests on Friday and Saturday nights and were accompanied by a 43-percent reduction in drivers with a BAC of 0.10 percent or more, a 15-percent reduction in all traffic accidents on weekend nights, and a 10-percent reduction in weeknight accidents. In Charlottesville, during a checkpoint set up from 11:30 p.m. to 4 a.m. nearly every Friday and Saturday night for 1 year, officers inspected drivers' licenses and looked for signs of intoxication during brief interviews. Although a 12-percent reduction in nighttime accidents and a 15-percent reduction in all police-reported, alcohol-related accidents occurred during the year, the results were not found to be statistically significant after statewide trends and seasonal variations were considered.

The differences in scheduling of blitzes in Stockton and Charlottesville may have influenced the relative success of the intervention in the two cities. Further research will be required to determine if periodic repetition of police blitzes is more effective in reducing accidents than continuous application of this deterrent measure over a long period of time.

It should also be noted that, although evaluations of deterrence programs in individual States have varied in their conclusions about the effectiveness of these programs, the results of a recent national study of the effects of laws against alcohol-impaired driving which combined State data indicated that "per se" laws that define DWI using BAC thresholds, administrative suspension or revocation laws, and laws that mandate jail or community service for DWI first offenders each played a role in the decline in fatal alcohol-related crashes in the early 1980s (Zador et al. 1988). Administrative license suspension and revocation and mandatory jail or community service contributed to a reduction of crashes during evening, late night, and early morning hours when alcohol involvement in fatal crashes is most likely. "Per se" laws were associated with a decline in crashes during daytime hours when alcohol involvement in fatal crashes is lower. It was estimated that, in 1985, 1,560 fewer drivers were involved in fatal crashes because of these three types of drinking-and-driving laws (Zador et al. 1988).

Education as an Alternative to Legal Sanctions for DWI

In most States, drivers found guilty of DWI can choose to participate in alcohol education or rehabilitation programs as an alternative to court-ordered punitive sanctions such as fines, jail sentences, or license revocation (National Transportation Safety Board 1987). Drivers arrested for DWI offenses may be referred by the court to education or intervention/treatment programs as alternatives to legal sanctions like suspension or revocation of driver's licenses. Offenders experiencing adverse effects of alcohol use are generally referred to intervention programs; drivers classified as social drinkers have been referred to education programs. (A discussion of identification of alcohol-related problems among individuals arrested for impaired driving as a means of initiating early intervention or referral to treatment is found in chapter X.)

The value of referring drivers to alcohol education programs is based on two assumptions: One is that drunk driving occurs because drivers lack knowledge about the effect of alcohol on driving and the circumstances leading to and consequences of drunk driving and do not understand their own drinking habits or how to modify them; the second is that education on these topics will produce positive attitude changes and thereby decrease drunk driving and alcohol-related traffic accidents as well (Klajner et al. 1984).

A review of the results of experimental evaluations of education programs for drinking-driving offenders suggested that, although these programs appear to improve knowledge and attitudes about drinking and driving, their effects on personal alcohol consumption and alcohol-related problems appear to be minimal (Mann et al. 1983). Moreover, experimental studies have not consistently demonstrated that these programs have any strong impact on repeated impaired driving or other hazardous driving behavior (Mann et al. 1983; Peck et al. 1985).

A recent 4-year followup study (Perrine and Sadler 1987)—the most recent of a series of studies (Hagen 1977; Hagen et al. 1980; Sadler and Perrine 1984) comparing California DWI offenders who received license actions with drivers referred to rehabilitation programs—found that offenders who received license actions had fewer crashes than those who were referred by the court to rehabilitation programs, although neither approach had much effect on rearrest for DWI (Perrine and Sadler 1987). However, in view of the limited evidence on the effectiveness of education programs in modifying driving behavior, and because license actions have been found to have a positive impact on traffic safety outcomes unrelated to alcohol, it has been argued (Mann et al. 1983; Hagen 1985; Donovan in press; Peck et al. 1985) that education programs would be more appropriate as a supplement than as an alternative to revoking or suspending the license (actions that appear to be more effective in deterring subsequent crashes).

Interaction and Differential Impact of Policy Measures

Although the effects of higher prices for alcoholic beverages, minimum-drinking-age laws, drinking-and-driving laws, and regulations affecting the availability of alcohol have been studied independently, it is very probable that these policy measures interact with one another in their impact on traffic accidents (Farrell in press). Furthermore, it can be expected that these measures will differentially affect drinking drivers—for example, different effects may occur based on age, gender, or socioeconomic status of drinking drivers as well as on factors specifically related to their driving or drinking (Farrell in press). An accurate understanding of the role of various policy measures in influencing accidents will require further research into these interactions and differential effects.

The interaction among drinking-and-driving policy measures, related events (such as promotions in the media about increased penalties for DWI), and other policy measures must also be considered (Hingson et al. 1988). For example, Hingson et al. (1987) reported that the sharp initial declines in fatal crashes following the implementation of Maine's 1981 comprehensive drunken-driving laws were compromised by a shift in police enforcement away from enforcement of speeding laws after the enactment of the 1981 laws. Research findings also suggest that the level of publicity influences the impact of law enforcement efforts (Ross 1984, 1987a,b; Mercer 1985; Vingilis et al. 1988; Shore and Maguin 1988). Hingson et al. (1988) noted that it is unclear whether new cohorts of drivers entering the high-risk category of teenage drivers were influenced by the media attention and public discussion about drunken driving that occurred in the early 1980s. They reported some evidence suggesting that influence may have been reduced for this group: After several years of decline, there was a 17-percent increase in single-vehicle nighttime fatal crashes and a 6-percent increase in other fatal crashes for teenagers during 1986. Data from 1987 showed fewer single-vehicle nighttime fatal crashes among teenagers in 1987 than in 1986, but the total number of crashes remained 9 percent higher than in 1985 (Hingson et al. 1988). The authors argued that continued publicity efforts are required to heighten awareness among this group and to maintain the attention of the public at large on these issues.

Research in Tennessee by Decker et al. (1988), during a period when both increased penalties for DWI and a change in minimum drinking age to 19 years of age were implemented, suggests that effects on young people of different DWI prevention efforts and related publicity concerning these efforts may vary with age. Although an increased minimum drinking age had a strong effect in reducing fatalities among 19- and 20-year-olds, the threat of increased DWI penalties had no effect. However, a large effect of increased penalties lasted for almost 4 years for 15- to 18-year-olds. The effect of publicity is suggested by figure 3, which compares annual number of articles on DWI in selected newspapers and magazines (McCarthy et al. 1988) with single-vehicle nighttime driver fatality rates for 15- to 18-year-olds.

Server Training

Although most establishments serving alcohol are subject to State or local liquor control laws that make it illegal to serve alcohol to individuals who are under age or visibly intoxicated, enforcement efforts primarily address the serving of alcohol to minors. Because of the difficulties of establishing enforceable standards for determining visible intoxication and of proving in court that intoxicated patrons have been served, establishments rarely have been cited for serving alcohol to an intoxicated patron (McKnight 1987). However, 35 States have "dram shop" laws that allow an individual injured by a driver who was served alcohol illegally while intoxicated to sue the server of the alcohol for recovery of damages.

Concern over a recent rise in dram shop suits has led the hospitality industry to educate servers, managers, and owners about practices that can reduce their liability and prevent alcohol-impaired driving (McKnight 1987). Server training

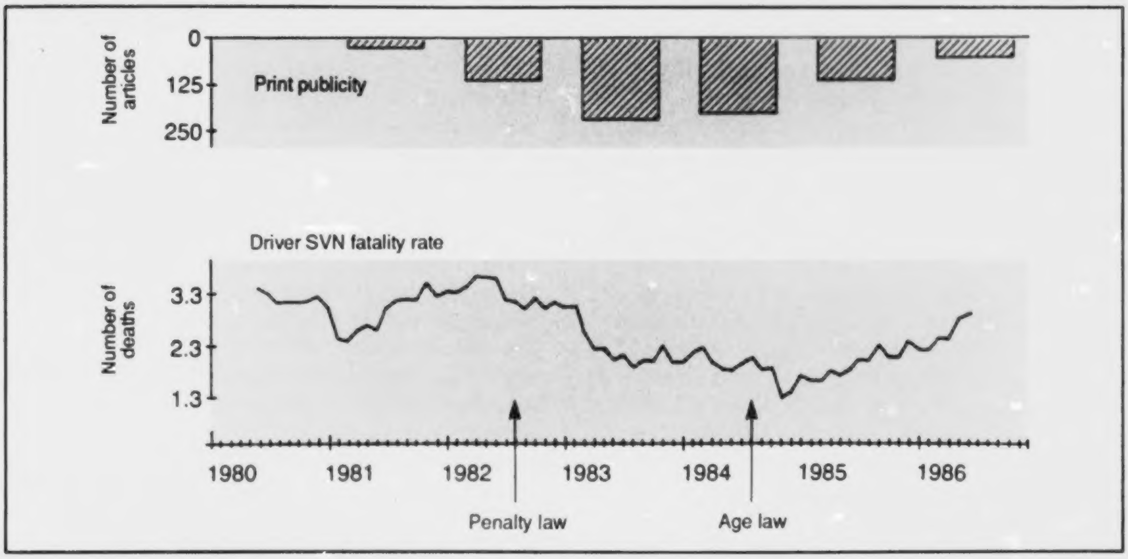


FIGURE 3. Measure of anti-DUI publicity and 12-month moving averages of monthly single-vehicle nighttime (SVN) driver fatality rates per 100 million vehicle miles for 15- to 18-year-olds.
SOURCE: Decker et al. 1988. Copyright 1988 by the American Medical Association.

is an attempt to modify the drinker's environment by changing the behaviors of alcohol servers in public establishments.

Saltz (1989) recently reviewed research on server training. Although this approach is relatively new, the few evaluations that have been reported are promising. Evaluations of servers' posttraining behavior suggest that training has a positive effect, including increased server efforts to reduce rate of consumption and amount of alcohol served (Geller et al. 1987; Russ and Geller 1987), on the amount of alcohol consumed by patrons (Geller et al. 1987; Russ and Geller 1987), and on the probability of patron intoxication (Saltz 1987).

One study found that the probability of a customer's becoming intoxicated was cut in half —although per capita consumption did not change—after servers had been trained to monitor for potential intoxication based on amount of alcohol consumed, rate of consumption, and customer weight (Saltz 1987). Another study (Geller et al. 1987) monitored servers' behaviors while serving research staff members posing as patrons; the pseudopatrons served by a trained server had lower BACs (see fig. 4). During Training for Intervention Procedures by Servers of Alcohol (TIPS), servers were given information on the physiological effects of alcohol that could help them identify specific warning signs of overindulgence, and they were taught a variety of tactics for dealing with customers who are intoxicated or approaching their limits. Slight increases in trained servers' efforts to slow down the rate of alcohol consumption and decreases in the amount of alcohol served were also observed when these servers were compared to untrained servers.

An example of a community-based program emphasizing server training is the Techniques of Effective Alcohol Management (TEAM) project, a collaboration of NHTSA with the International Association of Auditorium Managers, the National Basketball Association (NBA), GEICO Insurance Company, the National Automobile Dealers Association, the National Safety Council, the Motor Vehicles Manufacturers Association, and CBS Television (NHTSA 1986). Sports facilities are focal points of activity for the TEAM program, which attempts to create a more enjoyable game atmosphere with effective crowd control and to reduce threats to patrons and residents of the surrounding communities by decreasing drunk- and drugged-driving incidents after sporting events (Dickman 1988). A TEAM demonstration project, conducted in seven arenas where NBA teams play, provided training and disseminated information about responsible sales, service, promotion, and consumption of alcoholic beverages in public assembly facilities (NHTSA 1986). Workers in beverage and food services, indoor security, ushering, parking lot security, and ticket handling were trained to

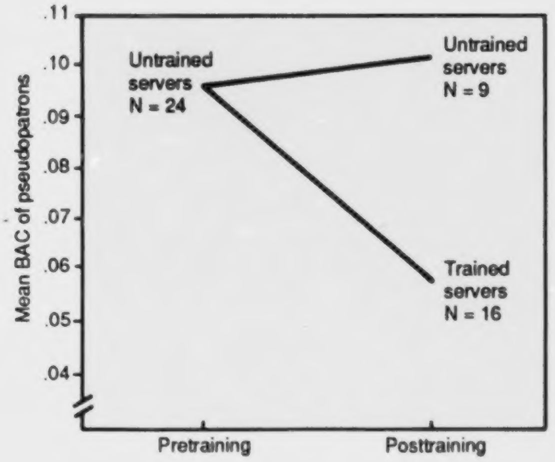


FIGURE 4. Mean BAC of pseudopatrons by server training status.
SOURCE: Geller et al. 1987.

recognize and intervene with individuals showing signs of alcohol impairment. Transportation alternatives, such as designated driver programs, were instituted and promoted. Activities to increase public awareness of alcohol traffic safety, such as flashing traffic safety messages about drinking and driving on arena scoreboards, were also initiated. By the end of 1987, TEAM training had been conducted for staff of 44 sports facilities (NHTSA 1988c). A strict evaluation design was not employed in the TEAM demonstration project; further evaluation of the impact of this comprehensive approach to prevention appears warranted.

Two recent studies of server training programs suggest that program success may be related to the degree of support given to these programs by managers of establishments that serve alcohol or by other significant members of communities in which such programs are implemented (McKnight 1987; Wittman in press). In an evaluation of a communitywide server training program conducted in two cities, McKnight (1987) observed increases in server actions designed to reduce alcohol consumption and prevent driving by pseudopatrons feigning intoxication, but only in the city where management policies for such server practices had been improved. The investigator suggested that the servers' performance may be related to management support. Wittman (in press) reported that server training and other strategies designed to prevent alcohol use problems at fraternity house social events were accepted and implemented by students at a large university, but resistance to the program by fraternity alumni advisors thwarted attempts to monitor and evaluate these activities and restricted further program development. Such potential obstacles indicate a need for early proactive efforts to involve all relevant community members in program planning (Wittman in press).

Because servers can tailor their actions to specific drinkers, their efforts may be more influential than public service announcements directed at large segments of the population (Geller et al. 1987). Also, because server practices have the potential to affect drinking that occurs immediately before driving, they may be more effective than standard prevention education approaches, which are removed in time from drinking-and-driving situations (Geller et al. 1987). Further investigation is required to understand the environmental factors, management policy, serving behaviors, and training practices related to effective server training initiatives (Geller et al. 1987).

Motor Vehicle and Roadway Design

One motor vehicle design feature that is directly related to the reduction of alcohol-related fatalities is the ignition interlock device, which prevents an individual who is intoxicated from operating an automobile. These devices, currently used primarily with DWI offenders, use breath-test technology and have gained recent attention as they have become more reliable and accurate and have incorporated features that prevent or detect many forms of tampering or circumvention (NHTSA 1988b). Evidence is not currently available, however, to judge the potential effectiveness of these devices to deter alcohol-impaired driving.

Motor vehicle and roadway design features capable of reducing all motor vehicle fatalities would also influence alcohol-related traffic fatalities. Waller (1989) recently discussed features of design that may contribute to or prevent crashes, as well as features that may increase or reduce the severity of crashes. Vehicle modifications include elevated rear brake lights (Waller 1989), passive restraints such as self-fastening seat belts and air bags, penetration-resistant windshields, padded dashboards, and other energy- and injury-absorbing features (Cameron 1979; Vingilis 1985). Road design factors related to crashes include the dimensions of grades and curves (Wright and Robertson 1976) and the speed at which traffic lights change from green to red (Zador et al. 1985). Nedas et al. (1982) found that when the width of stripes painted in the road was increased, impaired drivers were less likely to wander off the sides of roads or across the center line.

Transportation Alternatives

Apsler (1989) recently discussed two strategies that provide transportation alternatives for drinkers: designated drivers and ride service programs. A 1987 Gallup Poll (Gallup 1987) found that 78 percent of individuals who visit settings where alcohol is served would be willing to serve as designated drivers, that is, to remain sober and drive others in their group who were intoxicated. No research has been done to evaluate the effectiveness of this tactic in preventing crashes. Although some formal designated driver programs have been established—primarily by bars and restaurants—survey data suggest that this strategy is used mostly informally by groups of drinkers (Apsler 1989; Apsler et al. 1987).

The ride service program, also frequently known as the safe ride or dial-a-ride program, attempts to reduce alcohol-related traffic accidents by providing intoxicated drivers with alternative transportation. Harding et al. (1988) recently identified 325 ride service programs across the country, operated by types of organizations such as cab companies, bus companies, charitable organizations, trade associations, hospitals, and government agencies such as police departments. Two-thirds of these programs transport intoxicated drivers by taxicab, and 95 percent provide their services at no cost to the rider. On the average, the programs deliver 841 rides per year, and the number of riders served is estimated at 1.5 times this figure (Harding et al. 1988). A survey by Caudill et al. (in press) of bar and nightclub patrons in Sacramento and San Jose, California, indicated that although more than one-third of the patrons had not heard of ride services and few had used them, 79 percent said that they might use such a service if it were available; 87 percent of heavy drinkers reported that they might take advantage of such a service.

Rigorous evaluations to determine the impact of ride service programs on traffic safety are virtually nonexistent. Although such programs often are supported and endorsed by groups like Mothers Against Drunk Driving (MADD) and by police departments, half the programs studied by Harding et al. (1988) were opposed by individuals or small segments of the community who charged that these programs promote drinking. Data documenting this possibility also are not available, and the issue had not seriously threatened most of the ride service programs studied (Harding et al. 1988).

Measures to Change Individual Behaviors

Prevention strategies aimed at changing individual behaviors have been delivered through school- and community-based programs and through mass media campaigns. Traditional mass media programs to educate the general public and prevention education programs for school-age children and youths have emphasized the transmission of information about alcohol and alcohol-related problems with an underlying assumption that this information would lead to changes in attitudes and behavior. In general, research on the effectiveness of mass media campaigns that attempt to influence health behavior by transmitting information has found positive but low correlations between knowledge or attitudes and behavior (Bettinghaus 1986). In line with these general findings, studies investigating mass media campaigns to prevent alcohol-related problems also have found that information transmission approaches have had limited or no effects on behavior (Hewitt and Blane 1984). Reviews of attempts to influence alcohol-related behaviors of children and youths by transmitting information in alcohol education programs also continue to conclude that these programs generally have been ineffective (Rundall and Bruvold 1988). Recently, prevention programs based on the social learning model that emphasizes the role of peers in alcohol and drug use have been targeted at children and youths, but more research will be required to measure and understand the impact of this approach.

Programs for School-Age Children and Youths

Prevention activities for school-age children and youths are frequently school based, but they also may be operated at other sites such as Boys' Clubs, YMCAs, recreational centers, and public housing developments. Although many such programs emphasize didactic education on alcohol-related topics, prevention programs also offer youths positive alternatives to drinking and attempt to strengthen skills that will help young people resist pressures to drink. These programs may focus on general prevention of alcohol use or they may be based in driver education programs for youths and emphasize preventing drinking and driving.

General Prevention of Alcohol Use. For the most part, prevention programs have attempted to delay onset of alcohol use among youths with one or more of the following approaches: increasing knowledge and changing attitudes, teaching values and decisionmaking skills, or developing peer refusal and social competency skills. Evaluations of these programs have found that most approaches appear to have a positive effect on knowledge (Rundall and Bruvold 1988), but there has been little consistent evidence suggesting that specific approaches change attitudes or delay or prevent alcohol use (Moskowitz 1989). In line with the findings of previous reviews of prevention research, a number of long-term evaluations of prevention programs for children and youths recently have reported limited or no impact on alcohol use (Schaps et al. 1986; Hopkins et al. 1988; Duryea and Okwumabua 1988; Hansen, Malotte, and Fielding 1988).

Hopkins et al. (1988) evaluated a comprehensive program for elementary through high school students, which was designed to increase knowledge and build appropriate attitudes about alcohol, enhance self-esteem, and teach decisionmaking skills. In 2- and 3-year followups, the study found no consistent evidence of program impact on students' use of alcohol, cigarettes, or other drugs. In a further analysis of study data, Hopkins and his associates (Mauss et al. 1988) found that the variables that were addressed in the program—and that most often were the focus of school-based alcohol education programs in general (such as knowledge and attitudes about alcohol, decisionmaking skills, and self-esteem)—had limited influence on the drinking behavior of students. More influence on drinking behavior was found to be attached to noncurricular variables—that is, characteristics that students bring with them into a program and that usually are not or cannot be addressed by school-based interventions. Examples are demographic characteristics, such as religion, and variables such as relationships with peers and parents. The authors suggested that a focus on those noncurricular variables that are amenable to change, such as factors related to students' relationships with parents or peers, may be more effective in preventing alcohol use than the focus on cognitive, attitudinal, and affective variables that is currently emphasized in school-based programs.

Planners of prevention programs for children and youths recently have used Bandura's (1977) social learning theory as a basis for program development (Johnson et al. 1988). According to this theory, people learn about the positive and negative consequences of specific behaviors both through their own experiences and through observation of other people. Early research testing this theory found that children imitate others whose behavior receives support.

Prevention programs based on social learning theory, sometimes labeled "social influence" programs, emphasize the role of peers in alcohol and other drug use. Such programs—which, in some instances, are taught by peers who have positive status—stress peer refusal skills, correct normative expectations about alcohol and other drug use, sensitize young people to inaccurate messages about drinking promoted by advertising and other media portrayals of alcohol, and provide information about parental and other adult influences (Hansen, Johnson, et al. 1988). Some programs growing out of social learning theory often use a cognitive-behavioral approach (Botvin and Wills 1985) that combines social influence strategies with interventions intended to improve general coping skills and thereby reduce factors like low self-esteem and self-confidence, which potentially may motivate alcohol use. A focus on the latter skills has been labeled an affective education approach and may include training that focuses on enhancement of self-esteem and self-image, stress management, values clarification, decisionmaking, and goal setting.

Social learning theory has been the basis for a number of school-based smoking prevention programs. A review of 17 school-based smoking prevention programs based on the social learning model suggested that this approach helps prevent the onset of smoking (Flay 1985). However, the pattern of results across and within studies of these programs is inconsistent, and little is known about the programs' long-term effects on smoking prevention (Moskowitz 1989). When social learning theory has been applied in programs for preventing alcohol use, some studies have shown positive effects (Hansen, Johnson, et al. 1988; Dielman et al. 1989; Botvin, Baker, Botvin, et al. 1984; Botvin, Baker, Renick, et al. 1984; Gilchrist et al. 1987; Wodarski 1987; Perry and Grant 1988; Perry et al. in press), but other research has found very limited or no impact (Hansen, Malotte, and Fielding 1988; Duryea and Okwumabua 1988; Schaps et al. 1986). It has been suggested that the apparent success of this approach in smoking prevention may be related to the current social climate and general belief that people should not smoke (Moskowitz 1983); lack of similar attitudes about alcohol may reduce the impact of this and other educational approaches attempting to prevent alcohol use among children and youths (Moskowitz 1989; Rundall and Bruvold 1988).

Two recently reported studies found that programs emphasizing a social influences approach had no long-term preventive impact (Hansen, Malotte, and Fielding 1988; Duryea and Okwumabua 1988). Duryea et al. (1984) found that Nebraska ninth-graders who had participated in a social influences program and were tested 2 weeks and 6 months afterward showed more knowledge about the consequences of alcohol use, were better at refuting inducements to drink and drive, and were less likely to comply with pressure to participate in alcohol-related situations or to ride with drinking drivers compared to students who had not participated in the program. However, a followup of these students 3 years after program participation (Duryea and Okwumabua 1988) found no differences between participants and controls in their reports of drinking frequency or accompanying drinking drivers. In 3- and 4-year followups, Hansen, Malotte, and Fielding (1988) found that a social influences program delivered to Los Angeles sixth- and seventh-grade students by classroom teachers and peer opinion-leader assistants had no effect in reducing onset or prevalence of alcohol use when compared to controls who did not participate.

Results of some evaluations of programs based on the social learning model suggest that this method may not have long-term effects in preventing onset of drinking but may reduce the amount of drinking among young people (Hansen, Johnson, et al. 1988; Dielman et al. 1989; Botvin, Baker, Renick, et al. 1984; Botvin, Baker, Botvin, et al. 1984). For example, a program for seventh-graders in New York City using a cognitive-behavioral approach did not prevent or delay early use of alcohol, but study results indicated that participating children reported less frequent drinking, less alcohol consumption when they drank, and fewer episodes of drunkenness than the control group at a 9-month followup (Botvin, Baker, Botvin, et al. 1984).

In a study of fifth- and sixth-graders in Michigan (Dielman et al. 1989) who had been randomly assigned to a peer-resistance program, followup at 2, 14, and 26 months found that children who had participated in the study in sixth grade and who had used alcohol in both supervised and unsupervised contexts before participating had a reduced rate of increase in alcohol use, compared to a control group of children who did not participate. The program did not change the rate of increase of use among children who had had only supervised use before participation, and it did not delay the onset of use or affect alcohol use patterns of children who were abstainers before participation. No effects were found for children who had participated in the program as fifth-graders.

The cognitive-behavioral model was adapted for use with American Indian students in the Pacific Northwest (Gilchrist et al. 1987). The program focused on decisionmaking and skills needed to resist overt and covert pressures to use alcohol and other drugs. It also included discussion of culturally relevant material such as myths about reasons why American Indians drink, factors that encourage alcohol and other drug use among Indians, and thinking skills needed to maintain the "Indian way" and to avoid using alcohol and other drugs. A 6-month followup indicated that program participants had lower rates of self-reported alcohol, marijuana, and inhalant use than a control group.

Another program combined the cognitive-behavioral approach with the "Teams-Games-Tournaments" (TGT) technique (Wodarski 1987), in which students were placed on ability-matched teams that competed in tournaments of skills and knowledge about the consequences of alcohol. In the TGT approach, rewards are based on group rather than individual performance. Students in the 9th, 10th, and 11th grades randomly assigned to the cognitive-behavioral-TGT approach were compared to groups receiving traditional alcohol education or no instruction. Students who were taught with the combined cognitive-behavioral-TGT approach showed significantly greater knowledge about alcohol, decreases in self-reported drinking behavior, a more negative attitude about drinking and driving, and use of more alternative behaviors for avoiding driving after excessive drinking. Followups at 1 and 2 years indicated that the cognitive-behavioral-TGT group had maintained these changes in knowledge, attitudes, and self-reported behavior and that the differences between this group and the control groups also were maintained (Wodarski 1987).

The results of one study that directly compared the impact of the two components of the cognitive-behavioral model—the social influences and affective education approaches—suggested that when the two approaches were conducted independent of each other, the social influences approach reduced alcohol use among children who participated as seventh-graders, whereas the affective approach did not reduce alcohol use and even may have increased it (Hansen, Johnson, et al. 1988). In a 1-year followup, children in the social influences program showed reduced prevalence of alcohol, tobacco, and marijuana use compared to a control group that did not participate; children who were nonusers before participation showed a reduced probability of onset of use of the three substances. At a 2-year followup, initial nonusers in the social influences program were less likely than controls to report drinking two or more drinks during the past 30 days, but there were no significant differences between these two groups at lower levels of drinking. Those children who were users before participating showed reduced use of alcohol at the 1-year followup, but this difference was not maintained at 2 years. The affective program showed no preventive impact on children, and at the 2-year followup, alcohol use was greater by affective program participants who were users before participating than by social influence participants and the control group. Further research will be required to compare the combined effects of the social influences and affective approaches that are used in the cognitive-behavioral model with the impact of each type of program when conducted independently (Hansen, Johnson, et al. 1988).

The results of studies of social influences programs that have directly investigated the effect of actual peer involvement in the instruction process suggest that peer involvement may increase the impact of these programs (Botvin, Baker, Renick, et al. 1984; Perry and Grant 1988; Perry et al. in press). Botvin, Baker, Renick, et al. (1984) evaluated a prevention program for seventh-graders in New York suburban junior high schools based on a cognitive-behavioral model. Decreased use of alcohol, tobacco, and marijuana was found for children randomly assigned to the program compared to children not in the program, when the program was taught by trained high school students; this reduction was not found when classroom teachers served as program instructors.

An evaluation conducted in Australia, Chile, Norway, and Swaziland by the World Health Organization (WHO) also compared peer-led and teacher-led social influences programs (Perry and Grant 1988; Perry et al. in press). In the peer-led condition, peer leaders were responsible for presenting about 70 percent of the curriculum and teachers presented the remainder. In the teacher-led condition, teachers were responsible for presenting the entire curriculum. The content of the peer-led and teacher-led curricula was identical. Although patterns of results differed across countries, this pilot investigation found that students in peer-led programs demonstrated significantly lower alcohol use scores in posttests conducted 1 month after the conclusion of the program than students in nine schools with teacher-led programs or the six control schools; in all of the participating countries, neither the teacher-led program nor the control group demonstrated more positive outcomes than the peer-led program for any outcome measure (Perry et al. in press). The investigators suggested further investigation including a greater number of countries, a longer followup period, and an assessment of variables that predict alcohol use among students (Perry and Grant 1988).

Schaps et al. (1986) summarized the results of a series of evaluations of seven school-based prevention strategies implemented in Napa, California, suggesting only a limited positive effect of a program using a cognitive-behavioral approach. The programs evaluated included a drug education course for seventh- and eighth-graders based on a cognitive-behavioral model (combining the social influences and affective approaches) and two alternatives programs (cross-age tutoring and operating a school store). Also evaluated were the impact on students of four in-service teacher-training programs focusing on classroom and individual factors that are thought to influence students' attitudes toward school, self-esteem, and social competencies. Each group of students was exposed to only one of the programs. Of all programs evaluated, only one version of the drug education program showed a positive, but short-term effect on alcohol use; it was confined to seventh-grade girls.

Because many prevention studies targeted at children and youths show very small or no measurable effects, and because there are inconsistencies and contradictions among outcomes of many prevention programs, it has been difficult to reach conclusions about these interventions. To assist in determining the effectiveness of various prevention approaches, meta-analytic techniques recently have been used to estimate the average effect of all broadly similar interventions by aggregating the results of a number of studies. Two meta-analyses have provided some evidence suggesting that programs that use innovative interventions such as emphasizing peer resistance skills or offering positive alternatives to drinking have some impact on alcohol use among young people (Rundall and Bruvold 1988; Tobler 1986). A meta-analysis conducted by Bangert-Drowns (1988) did not find differences in behavioral outcomes as a function of program type, but it did find that programs conducted by peer leaders had a larger effect size on attitudes about alcohol and other drugs than programs administered primarily by adults.

School-Based Driver Education Classes. Recent reports have reviewed evaluations of school-based programs for the prevention of drinking and driving, many of which are part of high school driver education classes (McKnight 1986; Mann et al. 1986; Vegega and Klitzner 1988; Klitzner 1989). After the establishment of many of the early driver education alcohol programs as part of the Alcohol Safety Action Projects of the early 1970s, almost every State has incorporated alcohol education into its driver education curriculum (McKnight 1986).

In addition to educational programs, other approaches designed to prevent youths from drinking and driving attempt to modify the environment by providing alternatives to drinking, such as alcohol-free events; transportation alternatives for intoxicated young drivers; incentives for reducing alcohol consumption; and regulation of the hours, places, and conditions under which alcohol will be served (McKnight 1986). However, although many youth-targeted programs that make such environmental alterations have been implemented, few have been evaluated (Williams 1987; Williams et al. 1986). Further research is required in this area.

None of the research on educational programs to prevent youths from drinking and driving has used traffic safety measures to assess program impact. Although traffic safety would be the most direct measure of a program's success, large study groups would be required because, despite the relatively high percentage of alcohol-related automobile accidents involving young people, the average teenager has a very low probability of being arrested for drinking and driving or being involved in an accident because of drinking (McKnight 1986). A means of addressing this problem would be to develop other indexes that have known relationships to traffic safety measures (Mann et al. 1986). This approach was adopted by McKnight et al. (1979, cited by Mann et al. 1986), who compared knowledge, attitudes, and self-reported drinking and driving responses of students who participated in a school program with the responses of other youths who had known drinking-driving problems.

Most studies of alcohol education programs for youths focusing on drinking and driving have shown improved knowledge and attitudes about alcohol and its relationship to driving (Mann et al. 1986; McKnight 1986). Research that has included self-reported drinking-driving behavior as an outcome measure has been inconclusive. These studies found no effects of education (McKnight et al. 1979, cited by McKnight 1986), self-reports of less drinking and driving but more drinking (Albert and Simpson 1985), and more permissive attitudes about drinking and driving (Kohn et al. 1982).

Although McKnight et al. (1979, cited by McKnight 1986) found that an alcohol education program was ineffective in leading students to control their own drinking and driving, they did find that it increased students' efforts to intervene in the drinking and driving of their peers. This tendency of youths to intervene has been found to increase after youths participate in instructional programs that provide practice in intervention (McKnight and McPherson 1986). When youths were randomly assigned to a peer intervention training program or an informational alcohol education program, both programs led to improved knowledge and attitudes about drinking and driving, but only participation in the peer intervention training program was related to a significantly higher incidence of intervention with others' drinking and driving during a followup period. Further research will be necessary to determine whether interventions by students who have received this training is successful in reducing drinking and driving among their peers.

Kohn et al. (1982) randomly assigned high school driver education students to view one of three versions of a film; all of the films included the same basic information but differed in the seriousness of the consequences of drinking and driving depicted at the end. All experimental groups showed a significant gain in knowledge, but the film versions with very low- and high-threat endings produced more permissive attitudes toward drinking and driving on an immediate posttest. A 6-month followup, however, found no differences among the groups in knowledge or attitudes or in self-reported drinking and driving.

Fear appeals or "scare tactics" were used in many earlier drug and alcohol education programs (Kinder et al. 1980). Although a number of factors, including such variables as gender and self-esteem of subjects and credibility of the communicator, have been found to influence the effects of fear appeals (Kohn et al. 1982), in general these approaches have not been shown to be effective means of changing behavior patterns of drug and alcohol use (Kinder et al. 1980).

Although the results of the Kohn et al. (1982) study are in accord with previous research indicating that scare tactics are not effective and may even lead to the opposite of the intended outcomes, the findings of another recent study suggest that an opportunity to observe firsthand the adverse consequences of driving while intoxicated may be an effective prevention approach for youths (Bernstein and Woodall 1987). Randomly assigned middle school students either (a) received classroom alcohol education about the short- and long-term consequences of abuse of alcohol and other drugs or (b) participated in a program that provided exposure to real-life social and medical consequences of alcohol and other drug abuse through visits and interviews with emergency department and trauma center patients and their families in conjunction with classroom alcohol education emphasizing the social consequences of alcohol and other drug abuse. Those students who made hospital visits in conjunction with classroom education demonstrated increasingly greater perception of risk from driving under the influence of drugs or alcohol over an 8-month followup period compared to the control group that received only classroom education (Bernstein and Woodall 1987). Further research will be required to determine the factors responsible for the positive outcome of this approach with respect to attitudes and to examine its impact on behavior.

Community Education Approaches

Community education strategies include mass media campaigns attempting to change behaviors of individuals in an entire community or members of specific groups in a community, such as drivers. Other examples of approaches to community education are the activities of local grassroots organizations and the implementation of community-based programs designed to educate large segments of the public and to provide other services that can prevent alcohol-related problems. Generally, the term "community-based" is not used to label programs that are entirely school based.

Mass Media Campaigns. There is evidence that mass media campaigns about drinking and driving can increase public knowledge. A campaign conducted in Canada combining broadcast and print media with increased law enforcement produced knowledge gains (Vingilis and Salutin 1980). Another Canadian campaign that employed only the media resulted in knowledge gains as well as small positive changes in self-reported behavior (Pierce et al. 1975). A more recent mass media campaign conducted in Maine targeted teenagers with radio public service announcements in one region of the State (Kovenock et al. 1986). Compared to individuals in a similar but separate region of the State, teenagers in the targeted region were found to have more knowledge of State drinking-and-driving laws and reported a lower incidence of driving after drinking.

For the most part, however, research indicates that mass media campaigns alone do not change health behavior (Bettinghaus 1986). Nonetheless, such campaigns can increase awareness, change attitudes, and provide a context in which other strategies for behavioral change can succeed (Rootman 1985). Recent discussions of the role of mass media campaigns in the prevention of alcohol abuse have emphasized the need for integrated approaches such as linking mass media and school-based prevention programs (Flay 1986) or focusing on more accurate portrayals of alcohol in television programming and advertising in combination with mass media campaigns in order to change the "message environment" pertaining to alcohol (Wallack 1985).

Community-Based Programs. The term "community-based program" has several interpretations when used to describe alcohol abuse prevention. It can refer to grassroots or self-help prevention programs that are implemented by the citizens of a community, in contrast to programs that are led or directed by government or other institutions. The term can also describe initiatives that target a defined community—that is, an entire city or town—as the setting for a comprehensive program of prevention measures.

Although the targeting of whole communities has not been applied extensively to alcohol problems, community-based models that are used to address other health-related problems may provide direction for future programming in alcohol abuse prevention. Such an approach has been widely used in health promotion programs to reduce risk factors for cardiovascular disease such as a high-cholesterol diet, lack of exercise, and smoking. Findings of the Stanford Heart Disease Prevention Project, a landmark program of this type, indicated that positive health effects were longer lasting when intensive instruction and in-home counseling accompanied the mass media education campaign than when a mass media approach was used alone (Farquhar et al. 1981). Another model of community-based prevention is illustrated by a program promoting and training for breast self-examination (BSE) as a means of detecting cancer at an earlier stage (Worden et al. 1987). BSE training presentations were made to groups of women in Vermont communities, and mass media were used to increase community support. An evaluation of the program found increases in self-reported frequency and quality of BSE for these women compared to women in a control community with no BSE program (Worden et al. 1987).

One of the few attempts to evaluate a community-based approach to altering drinking behavior was reported by Wallack and Barrows (1982-83). One Northern California community was exposed to a mass media campaign focused on reducing overuse of alcohol, a community storefront effort that provided a series of educational meetings tailored to different groups in the community (e.g., PTAs and employees in work settings), and workshops for elementary and secondary school teachers. A second community was exposed only to the media campaign. Study findings indicated that residents of target communities increased in knowledge about alcohol compared to the control community not exposed to such efforts, but there were no changes in behavior (Wallack and Barrows 1982–83). Problems in program implementation were reported by the authors, including objections by State wine producers, which led to modification of television commercials, delay, and reduced exposure; also reported was a lack of coordination between the mass media effort and the community educational meetings.

A more recent community education program trained drinkers in three Vermont communities to monitor their BAC levels using drink calculators (cardboard wheels and wallet cards) distributed to customers at bars and other licensed beverage outlets (Worden et al. 1989). Study results suggested that distribution of the calculators combined with instruction in their use by trained service personnel at beverage outlets and demonstrations on television public service announcements may have reduced drinking among drivers. In another recent community project in New Zealand (Casswell and Gilmore 1989), community organizers worked with local organizations to stimulate discussion in the media about alcohol policy issues related to availability, price, and advertising. A media campaign emphasizing the reduction of heavy drinking among young men was also initiated. A project evaluation indicated that while there was a national trend toward support for liberalization of alcohol policies during the study period, this trend appeared to be inhibited in cities where one or both of the education approaches were implemented.

Implementation problems also were reported in a university-based program of server training reported by Wittman (in press) and in a multicomponent community-based prevention initiative in Canada that promoted prevention messages through the media and through professionals, provided counseling and education for heavy drinkers, and attempted to stimulate local initiatives relevant to alcohol-related policies and problems (Giesbrecht in press). Both authors stressed the need to involve relevant, significant community members and institutions in the planning of community-based programs.

The recent development of grassroots programs to prevent alcohol-related problems is another example of community-based programming. Through community organization, various groups such as MADD, Students Against Driving Drunk, and Remove Intoxicated Drivers have maintained high visibility for alcohol-related problems and stimulated community action and legislative activity to prevent drunk driving (Wallack 1985). McCarthy et al. (1988) reported that since these organizations began forming in the late 1970s, more than 400 local groups have been established nationwide. The development of the local grassroots movement and descriptive studies that have been conducted were recently reviewed by McCarthy and Harvey (1989). However, the measurement of the direct impact of grassroots organizations on traffic safety is a difficult task; no evaluations of the effectiveness of these programs in preventing drunk driving or reducing crashes have been reported in the literature.

Summary

Research investigating the relationship between the price of alcoholic beverages and alcohol use problems such as motor vehicle crashes continues to be one of the most promising research areas related to prevention. Evidence documenting the association of price increases and both the amount of alcohol consumed and resulting problems continues to accumulate.

The increase in the minimum drinking age from 18 to 21 has also been demonstrated to be an effective prevention strategy. The greatest reduction in fatal traffic accidents involving drunk drivers from 1982-1986 was among drivers aged 16–20 in States that had increased their minimum drinking age to 21, and research findings suggest that these changes may have a long-term impact on fatal accidents.

Recent research also indicates that communities may use planning and zoning ordinances to prevent alcohol use problems. Other research on alcohol availability indicates that factors such as type and number of outlets selling alcohol as well as the particular hours of the day alcohol beverages are available for sale can influence the amount of alcohol sold and the number and timing of automobile crashes.

Accumulating data indicate that implementation problems, including limited promotion in the media and law officers' low priority for programs designed to deter drinking and driving, may have reduced the impact of such measures. These findings suggest that short-term positive effects of deterrent programs may be viewed as promising results that call for improved implementation and further research into the long-term impact of these approaches.

Data on server training programs, a relatively new approach to reducing the incidence of drunk driving, are becoming available. Evaluations of these programs, though few in number, suggest that server training may increase server efforts to reduce rate of consumption and the amount of alcohol served and may decrease the amount of alcohol consumed by patrons and the probability of their intoxication.

It is possible that various alcohol-related policy measures interact with one another in their impact on traffic crashes and affect different groups of drivers differently. For example, research has shown that increased penalties for DWI have different effects for 19- and 20-year-old drivers as compared to those 15 through 18 years of age.

The results of recent prevention efforts focused on school-age children suggest that programs based on the social learning model may reduce alcohol use among young people. This approach provides children and youths with skills that they can use to resist pressures to drink and may involve peers in the instructional process. Other prevention approaches, such as those emphasizing alcohol education, have been found to increase young people's knowledge about alcohol and its effects, but generally have not been successful in changing attitudes or behavior.

Although there is some evidence that mass media campaigns can influence alcohol use problems such as drinking and driving, the need for community-based programming integrating mass media efforts into comprehensive efforts combining a variety of prevention measures continues to be an area of interest. While model community programs have been developed to address other health-related problems, few programs of this type have been implemented for the prevention of alcohol abuse. Available evidence suggests that successful implementation of such programs will require the involvement of significant community members and institutions in the program planning process.

The effect of advertising and other media portrayals of alcohol on consumption and alcohol-related problems continues to be an issue. It is clear that the portrayal of drinking on television programs presents an unrealistic picture of drinking that is unbalanced in its depiction of drinking frequency and outcome. Recent research also indicates that, while the amount of national alcohol advertising in college newspapers decreased between the late 1970s and the mid-1980s, during both periods the amount of advertising space devoted to alcohol advertising greatly exceeded advertising for books and soft drinks. However, due to the limited amount of research conducted in this area, it is not possible to draw firm conclusions about the influence of either alcohol advertising or other portrayals of alcohol by the media on alcohol consumption.

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■ *Chapter X*

Early and Minimal Intervention

Introduction

Early intervention targets nondependent drinkers—that is, individuals who are either at high risk for developing alcohol-related problems or who are experiencing adverse effects of drinking but who are not alcohol dependent. The intervention process includes both identifying such individuals and modifying their drinking patterns and their drinking-related behaviors and attitudes.

Candidates for early and minimal intervention may be identified in health care settings, at worksites, as a result of arrests for driving while intoxicated (DWI), or through recruitment campaigns using the mass media. Minimal intervention such as brief counseling or advice from a health care provider about alcohol-related problems is an area of growing research interest. Moderation training is another early intervention approach that may prove effective for alcohol abusers experiencing alcohol-related problems. Clinical and research interest in early and minimal intervention is relatively recent, and data in these areas are therefore limited.

This chapter begins with a brief discussion of the early identification process. Recent studies on minimal intervention approaches, moderation training, interventions for drinking drivers and children of alcoholics, and employee assistance programs (EAPs) are also discussed.

Early Identification

Early intervention approaches may be targeted at nondependent drinkers who are beginning to experience adverse effects of alcohol such as work impairment (e.g., lowered performance rating or loss of workdays), social disruption (e.g., departure of spouse or arrests for alcohol-related offenses), or physical harm (e.g., accidents or illness) (Polich and Orvis 1979).

Identifying these drinkers is less straightforward than detecting people who have more severe alcohol-related problems. Skinner (1986) noted that the identification process is more difficult when detection is attempted in the early stages of drinking problems. Figure 1 depicts the disorders associated with early and later stages of excessive drinking. After 10 to 15 years of such drinking, patients are likely to have the classic symptoms related to alcohol dependence. Although a wide variety of psychosocial and biomedical problems are potentially related to alcohol abuse at earlier stages, these problems lack diagnostic sensitivity because no one of them is found in all alcohol abusers. Further, these clinical signs or symptoms tend to occur relatively independent of one another (Skinner 1986).

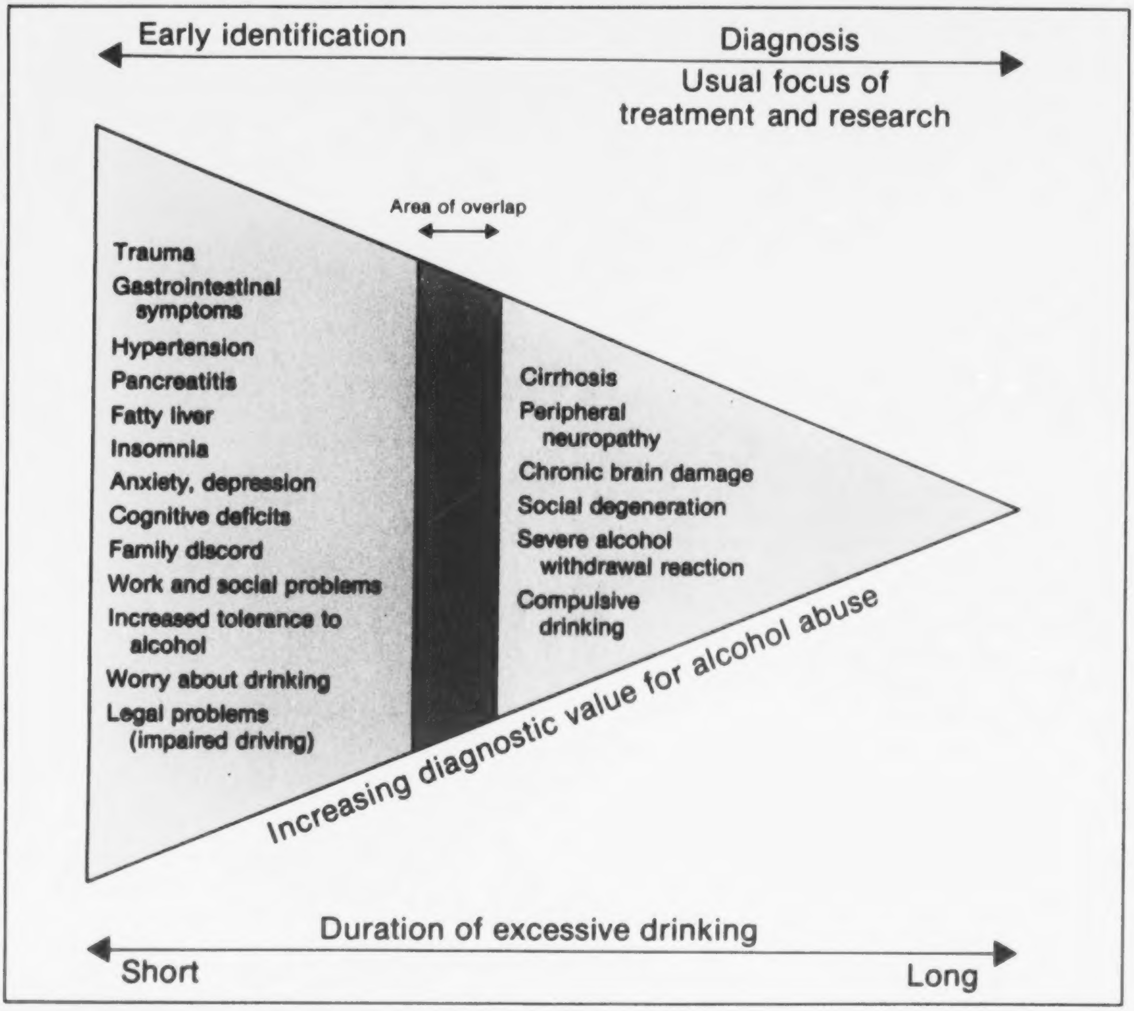
Early identification
Diagnosis
Usual focus of treatment and research
Area of overlap
Trauma
Gastrointestinal symptoms
Hypertension
Pancreatitis
Fatty liver
Insomnia
Anxiety, depression
Cognitive deficits
Family discord
Work and social problems
Increased tolerance to alcohol
Worry about drinking
Legal problems (impaired driving)
Cirrhosis
Peripheral neuropathy
Chronic brain damage
Social degeneration
Severe alcohol withdrawal reaction
Compulsive drinking
Increasing diagnostic value for alcohol abuse
Duration of excessive drinking
Short
Long

FIGURE 1. Disorders associated with the duration of excessive drinking.
SOURCE: Skinner 1986.

Because of such difficulties, persons in the early stages of alcohol abuse may not be identified in the course of routine diagnostic examinations. Furthermore, drinkers who seek help for their alcohol use problems may not do so until the problems are severe (Hingson et al. 1982). Consequently, a more proactive screening process is required to identify candidates for early intervention. Many health care settings have been proposed as appropriate for this screening, including primary care medical practices (Skinner et al. 1985a,b), general hospitals (Lewis and Gordon 1983), emergency rooms (Yates et al. 1987), and prenatal programs (Little et al. 1985). (A more detailed discussion of settings, instruments, and procedures for screening and diagnosis of alcohol use problems is in chapter VIII.) Alcohol use problems also may be identified at worksites or as the result of DWI arrests.

Evidence accumulated from evaluations of experimental alcohol intervention programs indicates that candidates for early intervention sometimes can be identified through relatively nonintensive recruitment efforts. A number of studies have reported that newspaper announcements and advertisements about programs are successful in encouraging self-referral by this population (Berg and Skutle 1986; Miller et al. 1980; Pomerleau et al. 1978; Sanchez-Craig et al. 1984; Vogler et al. 1977; W.R. Miller et al. 1988).

However, recruitment emphasizing self-referral may be less effective in programs for people with alcohol use problems than in programs for people with other types of problems. For example, the number of drinkers who self-referred to an experimental alcohol intervention program was approximately one-fourth the number of people who responded to similar recruitment campaigns for assertiveness training and stress management programs; campaigns for all programs used newspaper articles, radio and television shows, and visits to health and mental health agencies (Alden 1980). This result suggests that a large proportion of people with alcohol use problems in the general population may not be easily recruited into an early intervention program and would be unlikely to respond to a newspaper recruitment announcement. Research is needed to differentiate among those individuals who can and cannot be reached in this manner.

Early intervention efforts also may be targeted at people who are not yet alcohol dependent but who are at high risk for becoming dependent. Compelling evidence for a genetic contribution to susceptibility for alcohol dependence exists. Most offspring of alcohol-dependent parents do not, however, develop alcohol use problems. A substantial body of research documents efforts to characterize those at risk for alcohol dependence (see chapters III and IX). Such research may lead to the development of techniques to identify those most at risk for dependence.

Approaches to Early Intervention

Behavioral approaches to early intervention are a current emphasis. Some of these approaches are relatively complex and may involve a series of sessions over a period of weeks or months, but there is accumulating evidence that minimal interventions involving advice or counseling are also effective.

Minimal Intervention Approaches

Minimal intervention approaches have in common (1) low cost, (2) modest investment of time and resources, (3) emphasis on self-help and self-management techniques, and (4) minimal involvement of professionals (Babor et al. 1987). Current minimal intervention approaches build on the findings of research conducted in the 1970s in England, which suggested that a brief "advice" intervention, consisting of a 3-hour assessment followed by a 1-hour session of feedback and admonition, can be as effective as conventional treatment for nondependent drinkers experiencing adverse effects of alcohol (Orford et al. 1976). Since then, the effectiveness of minimal intervention has been examined in a number of countries.

The effectiveness of minimal interventions was investigated in Scotland with alcohol abusers who had been screened while hospitalized for non-alcohol-related reasons (Chick et al. 1985). A randomly selected intervention group received 30 to 60 minutes of counseling and a booklet of advice on reducing drinking. Control subjects received only routine medical care. At a 12-month followup, patients in the intervention group showed greater reduction in number of alcohol-related social and medical problems and in level of gamma-glutamyl transpeptidase (GGTP) activity, a measure of recent heavy alcohol use.

In a study in a New Zealand hospital (Elvy et al. 1988), randomly assigned surgical and orthopedic patients (nondependent drinkers who had screened positive for adverse effects of alcohol) were offered referral to an alcohol counselor at the hospital for further assessment and possible intervention or had no opportunity for referral. Letters giving screening and assessment results were also written to the general practitioners of referral group members. At 12 months, patients in the referral group showed greater improvement in self-reported drinking problems, as measured by a screening test developed to detect such problems in hospitalized patients (Elvy and Wells 1984). Referral group patients also had improved work performance, longer abstinence, and greater personal happiness than control patients. The referral group demonstrated continued, though more limited, improvement at the 18-month followup. The control patients generally showed no improvement, and some deterioration, in outcome variables at 12 months, but at 18 months they had marked improvement in drinking problems and some improvement on work and personal problems. The researchers believed that the 12-month followup with the control patients, conducted by a nurse, may itself have functioned as a minimal intervention and caused the subsequent improvement at 18 months.

The results of a screening and intervention program in Sweden also suggest that minimal interventions varying in intensity may influence certain drinking-related outcomes (Kristenson et al. 1983). Heavy and moderate drinkers with two consecutive GGTP values in the upper decile of the GGTP distribution were randomly assigned to an intervention group or control group. Members of the intervention group received quarterly consultations with a physician, monthly GGTP tests, and contact with a nurse. Counseling focused on living habits, and the goal was moderate drinking rather than abstinence. Members of the control group were informed by letter that they should restrict their alcohol consumption and were invited for additional measurements of their liver enzymes after 2, 4, and 6 years.

During the followup period, the intervention group had significant reductions in absences from work due to illness, days spent in the hospital, and mortality compared with the control group. However, GGTP values were significantly decreased in both groups at 2 and 4 years, and there was no significant difference between the two groups in the amount of reduction. Furthermore, there were no significant differences between the two groups in number of hospital days for alcohol-related conditions (alcohol psychosis, alcoholism, liver cirrhosis, and pancreatitis).

These results suggest that the letter received by the control group may have served as a minimal intervention that influenced outcomes related to drinking problems (GGTP level). Because the study did not include a control group receiving no intervention, however, it cannot be determined with certainty if the reductions in GGTP level for both study groups were related to the experimental intervention and the letter or to other factors. The significant reductions in absences from work due to illness, days spent in the hospital, and mortality for the intervention group coupled with the lack of significant difference between groups in number of hospital days for alcohol-related conditions also suggest that the quarterly consultations with a physician and monthly contacts with a nurse may have served a general health surveillance function for the intervention group.

In the United States, W. R. Miller and his associates found that the outcomes of drinkers who received a minimal intervention providing 3 hours of assessment, advice, and encouragement and a self-help manual based on behavioral self-control training (BSCT) did not differ from patients who received 6 to 18 weeks of individual BSCT therapy; all groups showed significant reduction in consumption (Miller and Taylor 1980; Miller et al. 1980; Miller et al. 1981; Miller and Baca 1983). Such findings suggested that advice and encouragement, the self-help manual, or the assessment process itself could act alone as a minimal intervention.

A recent study conducted in the United States by W. R. Miller et al. (1988) directly examined the possibility that a screening and assessment process could function as an effective minimal intervention. Miller and his colleagues studied the "drinker's checkup" (DCU), which includes (1) an interview to assess drinking pattern and history and life problems, (2) a blood test assayed for indicators of alcohol-related health impairment, (3) neurological tests of the effects of alcohol on the brain, (4) interviews with collaterals to confirm clients' self-reports, (5) an inventory of alcohol use, and (6) a followup session during which feedback of findings is provided.

Assessed subjects showed a modest but statistically significant reduction in alcohol consumption 6 weeks after their feedback sessions compared to control subjects who had not been assessed; assessed subjects maintained reduced consumption at an 18-month followup. However, 14 percent of the subjects sought help for their drinking problems within 6 weeks of feedback, and 33 percent sought help within 18 months of feedback. Although consumption was reduced, Miller and his colleagues concluded that the DCU alone was not sufficient intervention, because most clients had persisting symptoms and problems. They noted, however, that the DCU may provide a motivational boost and serve as preparation for treatment (W. R. Miller et al. 1988).

There have been relatively few evaluations of minimal interventions, but the results of the studies that have been conducted are promising. In a number of instances, unexpected findings have provided support for the concept of minimal intervention. For example, the "brief advice" given in the Orford et al. (1976) study, which generated initial interest in minimal intervention, was in fact intended to be a control condition and not anticipated to have a positive effect on outcome. The 3 hours of assessment, advice, and encouragement and self-help provided to subjects by W. R. Miller and his associates (Miller and Taylor 1980; Miller et al. 1980; Miller et al. 1981; Miller and Baca 1983) was also designed as a control condition. Outcomes of the Elvy et al. (1988) and Kristenson et al. (1983) studies also may have been influenced by interactions between health care providers and subjects that were not expected to have a therapeutic effect. Taken together, the results of this research suggest that the impact of any interaction between service providers and patients, however minimal, cannot be taken for granted. They also indicate the need for careful design of future research in this area—e.g., including no treatment control groups—so that the impact of various components of interventions can be independently evaluated.

Moderation Training

Recent reviews of the literature suggest that controlled drinking, as opposed to abstinence, is not an appropriate treatment goal for individuals who are dependent on alcohol (Miller and Hester 1986; Nathan and Skinstad 1987). It has been suggested, however, that training aimed at moderating drinking may be an effective intervention for nondependent drinkers experiencing adverse effects of alcohol (i.e., alcohol abusers) (Marlatt 1988; Miller 1984; Miller and Hester 1986; Nathan and Skinstad 1987; Ogborne 1987). Although findings have been mixed, research examining predictors of success indicates that the most consistent predictors of a positive outcome after moderation training have been lower duration and severity of drinking symptoms and problems (Miller and Hester 1986).

BSCT, the most frequently used approach for teaching moderate drinking, generally includes the following strategies (Miller 1984; Cellucci 1984): (1) setting specific limits and goals for drinking; (2) using biofeedback or a blood alcohol concentration (BAC) table or estimation rules to teach BAC discrimination; (3) self-monitoring of alcohol consumption; (4) slowing drinking through use of rate control methods; (5) using operant principles including self-reinforcement and self-contracting; (6) identifying frequent antecedents or consequences that affect drinking behavior; (7) altering antecedent conditions through stimulus control and teaching new skills such as drink refusal; and (8) learning behavioral alternatives to drinking.

The findings of research that has been conducted to evaluate the effectiveness of BSCT as an early intervention approach are inconclusive. BSCT has been found effective in reducing alcohol consumption by DWI offenders who were compared to untreated control subjects and to drivers placed in a conventional alcohol education program (Brown 1980). However, research conducted by W. R. Miller and his associates on nondependent, self-referred drinkers (Miller and Taylor 1980; Miller et al. 1980; Miller et al. 1981; Miller and Baca 1983) found that the proportion of successful outcomes did not differ between groups receiving 6 to 18 weeks of individual BSCT from a therapist and groups receiving a self-help manual on BSCT (Miller and Munoz 1982) plus 3 hours of assessment, advice, and encouragement. Although the results of W.R. Miller and his colleagues (Miller and Taylor 1980; Miller et al. 1980, Miller et al. 1981; Miller and Baca 1983) suggest that an intervention providing a BSCT self-help manual may be effective, further research is required to determine the relative effectiveness of therapist-conducted BSCT, BSCT provided by a self-help manual, or advice and encouragement alone.

It is possible that responses to these and other brief interventions may be differentially affected by patient characteristics. For example, Marlatt (1988) has proposed a "stepped-care" approach to intervention, based on a behavioral model of stages of change in habit acquisition and habit change that was developed originally by researchers in the field of smoking prevention and cessation (Prochaska and DiClemente 1986; DiClemente and Prochaska 1985). In the proposed approach, decisions about an appropriate intervention format would be based on the target individual's "change stage" and could vary in intensity ranging from use of a self-help manual or a single session of feedback and professional advice to comprehensive programs providing skill training (Marlatt 1988). (See chapter XI for a discussion of patient-treatment matching in more traditional alcoholism treatment programs.)

Intervening With Drinking Drivers

Arrests of drinking drivers may result in early identification of and intervention with their alcohol use problems. To increase the effectiveness of this identification and intervention process, the need to differentiate among individual drivers on the basis of their characteristics has recently been emphasized.

Intervening With DWI Offenders

Interventions for DWI offenders gained popularity when alcohol safety action programs were implemented in the United States (Klajner et al. 1984). These programs aimed to make client referrals based on assessment of the clients' actual problems. Because it was believed that the primary problem of DWI offenders was alcohol abuse rather than drunk driving, these drivers were referred to treatment programs instead of or in addition to educational programs (Klajner et al. 1984). In general, the DWI offenders referred to treatment programs have been the ones experiencing other adverse effects of alcohol use. Drivers classified as social drinkers have been referred only to educational programs. (See chapter IX for a discussion of the use of education programs to prevent further drunk driving among DWI offenders.)

Systematic research that documents the effectiveness of interventions on changing the drinking behavior of DWI offenders experiencing the adverse effects of alcohol is very limited. A review of research (Mann et al. 1983) indicates that group therapy and moderation training programs are the primary methods that have been evaluated experimentally. The findings of studies using a randomized control group suggest that moderation training may be more effective than group therapy in reducing drinking. Studies of programs using group therapy (Swenson and Clay 1980; Swenson et al. 1981) found no differences in drinking behavior between experimental and control groups, but such differences were found in a study that examined moderation training (Brown 1980). However, no direct comparisons of these methods have been made, and moderation training has not been widely applied as an intervention for DWI offenders.

Research on interventions for DWI offenders has also examined the impact of these interventions on rearrests for DWI. In a study conducted in 11 small Mississippi municipalities (Landrum et al. 1982, cited by Peck et al. 1985), there were no differences in DWI rearrests among DWI offenders randomly assigned to probation, group therapy, a combination of group therapy and probation, or a no-treatment control condition. However, Reis (1982, cited in Peck et al. 1985) found that Sacramento drivers randomly assigned to groups receiving (1) biweekly 15-minute interviews or (2) weekly 2-hour group therapy sessions had lower rates of DWI arrests during the year-long treatment period than the control group. During a 2-year followup period, however, the effect of the biweekly contact group on rearrest rates diminished more rapidly than the effect of group therapy; differences between the two groups began 2 months after the treatment period (Reis 1982, cited in Peck et al. 1985).

Furthermore, subject characteristics influenced the effects of the two types of interventions studied by Reis. For subjects with the educational equivalent of high school graduation or less, both the 15-minute biweekly contacts and group therapy were beneficial, whereas for subjects with 1 or more years of college, only therapy was effective. Neither intervention was more effective than the control condition for those subjects whose BACs were 0.19 or less at the time of their last DWI arrest, whereas both biweekly contact and therapy were more effective than no treatment for subjects whose BACs were 0.20 or greater; the latter did very poorly in the control group (Reis 1982, cited in Peck et al. 1985).

Although the interventions studied by Reis affected DWI arrests, they did not reduce the subjects' subsequent involvement in crashes. Furthermore, neither Reis nor Landrum et al. compared subjects receiving treatment to drivers who had their licenses suspended after DWI arrests. In many States, DWI offenders have the option of participating in educational or treatment programs as a substitute for court-ordered punitive sanctions such as license revocation or suspension (NTSB 1987).

Research conducted in California compared outcomes of DWI offenders in four counties where alcohol rehabilitation demonstration programs for drivers had been implemented, to outcomes of offenders in four matched comparison counties whose licenses were suspended or revoked (Hagen 1977; Hagen et al. 1980; Sadler and Perrine 1984; Perrine and Sadler 1987). At a 4-year followup, study findings indicated that offenders who received license actions had fewer crashes than those who were referred by the courts to rehabilitation programs (Sadler and Perrine 1984; Perrine and Sadler 1987).

Although these studies indicated that license action had a greater impact on traffic safety outcomes, neither rehabilitation nor sanctions had much affect on rearrests for DWI. In fact, sanctions reduced non-alcohol-related crashes and convictions, probably because drivers drove less, and more cautiously, during the period when they did not have valid driving licenses (Perrine and Sadler 1987).

It has been recommended that educational and intervention programs, because of their limited impact on traffic safety, should not be used with drunk drivers instead of license sanctions (Mann et al. 1983). However, arresting motorists for DWI offenses is an important means of identifying people with alcohol use problems and, through court diversion and supervision programs, of promoting their participation in interventions that address their drinking problems directly (NTSB 1987). It is important that DWI arrests continue to be a point of early identification and intervention. In this regard, research related to the efficacy of intervention programs and to the development of other effective means of involving DWI offenders in treatment is needed (Sadler and Perrine 1984). Further, research is needed involving the development of programs that combine the specific deterrent effects of license sanctions with the therapeutic impact of intervention programs so that both traffic safety and rehabilitative gains are possible (Donovan in press; Peck et al. 1985; Waller 1987).

Differentiating Among DWI Offenders

Although the need to consider the characteristics of individual DWI offenders has been emphasized as a means of improving the effectiveness of interventions (Perrine 1987; Selzer et al. 1977; Klajner et al. 1984), differential intervention planning for DWI offenders is virtually nonexistent (Klajner et al. 1984). Perrine (1987) suggested that successful differentiation among drinking drivers could lead to (1) early identification of potential DWI offenders, (2) more appropriate selection of DWI sanctions and court intervention referrals for particular offenders, (3) greater customization of intervention programs, (4) increased completion and compliance, and (5) lower rates of recidivism.

Recent research has differentiated among DWI offenders and among drinking drivers on the basis of personality and driving-related attitudes (Arstein-Kerslake and Peck 1985, cited by Perrine 1987; Donovan and Marlatt 1982), psychopathology (Mulligan et al. 1978; Snowden and Campbell 1986; Sutker et al. 1980), drinking-related variables (Snowden et al. 1986; Wilson and Jonah 1985, 1986, cited by Perrine 1987), and driving and general arrest records (Wells-Parker et al. 1986; Donovan and Umlauf in press). The findings of a number of these studies suggest that risk for DWI may be correlated with heavy alcohol consumption, a high number of arrests of various kinds, and a general tendency toward risk-taking behavior.

Wells-Parker et al. (1986) found that, of offenders referred to a probation and rehabilitation demonstration program, those who had the most DWI offenses also had the highest average number of arrests of other kinds, including public drunkenness, license violations, equipment violations, disturbances, and assaults. These drivers also had the highest recorded BACs.

Donovan and Umlauf's (in press) results suggest that high-risk or "bad" drivers who have had many traffic infractions and arrests but no DWI arrests may also be appropriate candidates for early intervention. During a 3-year followup period, 11.4 percent of these high-risk drivers were arrested for drunk driving compared to 2.0 percent of a sample of the general driving population. At an initial assessment before the 3-year followup, all the high-risk drivers were similar in demographics, personality functions (assertiveness, depression, emotional distress, locus of control, and sensation seeking), hostility, and risk-enhancing driver attitudes. However, those individuals who were later arrested for DWI consumed a greater number of drinks per month and were involved in more monthly occasions during which they consumed five or more drinks than other high-risk drivers.

These prospective findings of Donovan and Umlauf (in press) supported earlier findings of cross-sectional research by Wilson and Jonah (1986, cited by Perrine 1987) who conducted studies of drinkers who did not drive impaired, those who drove impaired but were not detected, and those who were convicted for DWI. Convicted DWI offenders had more prior accidents and convictions, drank more alcohol per occasion, and showed more symptoms of alcohol use problems than drivers who reported not driving impaired during the previous month or drivers who admitted driving impaired without being detected (Wilson and Jonah 1986, cited by Perrine 1987). Drinkers who admitted driving while impaired reported more violations and crashes, more alcohol consumption, and less seat belt use and were less likely to reduce their drinking at a party before driving than drinkers who reported not driving after drinking or those who reported driving after drinking but not when impaired (Wilson and Jonah 1985). The investigators suggested that driving while impaired may be part of a more global behavioral syndrome typified by high-risk behaviors and irresponsible attitudes (Wilson and Jonah 1985). As discussed in the following section on youthful drivers, Jonah and Dawson (1987) found evidence for the possibility of a "risk behavior syndrome" among young drivers (aged 16 to 24), but not among drivers in general.

Findings of Jaccard and Turrisi (1987) suggest that individuals' tendency for high-risk behavior may interfere with their ability accurately to assess drunkenness as measured by legal limits of blood alcohol. College students who were presented with hypothetical drinking scenarios perceived less impact of additional drinks on BAC as more drinks were consumed and were more likely to have this misperception for drinking scenarios that were described as 3 hours long than for those that were 1 hour long. Twice as many people made inaccurate judgments for beer as for mixed drinks. Further, although most subjects realized that having a large number of drinks would cause them to exceed the legal BAC, about 20 to 25 percent did not understand the impact of a moderate number of drinks. Subjects who scored higher on measures of risk taking and sensation seeking were more likely to make errors in judgment than subjects who scored higher on internal locus of control (the belief that they, not external events, control their fate). Jaccard and Turrisi (1987) suggested that interventions could be developed that address the types of cognitive errors made in assessing BAC and to counteract personality characteristics that increase the tendency to make such errors.

There is also evidence to indicate that individual drinking patterns may be differentially related to accuracy in ability to estimate BAC level and to judge whether a BAC level exceeds the statutory limit (Beirness 1987). Although the research literature indicates that most people's estimates while drinking do follow the pattern of their actual BAC as it rises and falls with absorption and elimination, they tend to be inaccurate in their estimations (Beirness 1984). Beirness (1983, cited in Beirness 1984) identified three types of BAC estimation error (see fig. 2) based on the direction of errors made by drinkers over a 3-hour experimental drinking session: (1) overestimates of BAC at almost every point in time; (2) "typical" or "mixed" patterns of estimation (Bois and Vogel-Sprott 1974), most often displayed by social drinkers, who overestimated their BAC during the absorption phase and underestimated it during the elimination phase; and (3) underestimates of BAC at all points in time.

Beirness (1987) found that underestimators' reports of usual drinking behavior indicated heavier consumption than that of the overestimators or drinkers with a mixed estimation pattern. Underestimators were also most likely to rate themselves fit to drive when their actual BAC was in excess of the statutory limit. The author suggested that, of the three groups, underestimators would be expected to benefit most from BAC discrimination training, which research (Vogel-Sprott 1975) has shown to reduce errors in BAC estimation and to enhance caution and concern about impairment after alcohol consumption.

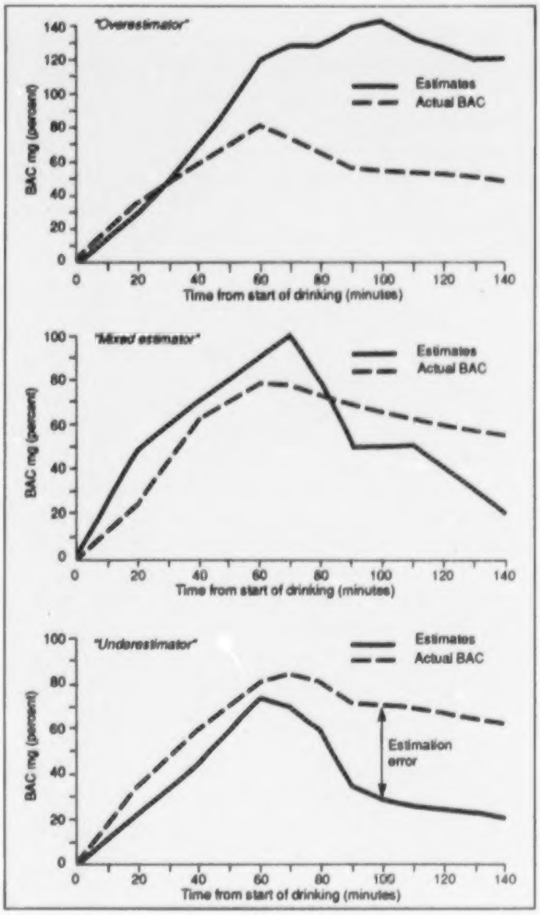

FIGURE 2. Actual and estimated blood alcohol concentration for an "overestimator," a "mixed" estimator, and an "underestimator."
SOURCE: Beirness 1984.

Taken together, the findings of these studies suggest that interventions for drivers at greatest risk of DWI should address a propensity for risky behavior and problems in estimating BAC as well as heavy alcohol consumption. Further research will be required to determine the impact that these data may have on the effectiveness of early identification and intervention efforts.

Intervening With Youthful Drivers

About 40 percent of all teenage deaths occur in traffic crashes (NHTSA 1988), and drivers under the age of 21 have the highest rates of alcohol-involved fatal crashes (Douglass 1982).

Little research has been conducted to examine the interrelationships among age, alcohol use, and other factors such as personality and social characteristics of young people who drive or have crashes after drinking (Mayhew et al. 1986; Lightsey and Sweeney 1985). In one of the few studies to examine such factors, Lightsey and Sweeney (1985) found that youthful DWI offenders, aged 15 to 24, who have a high level of alcohol-related problems (family, psychological, social, legal, economic, and physical) were more likely to drink to relax, cheer up, forget worries, and gain courage and to drink when they were lonely, angry, or nervous than were young people who had low or moderate levels of alcohol-related problems. Farrow (1987a) also found that young DWI offenders were more likely to use risky driving as a stress management technique than were nonoffenders. In addition, recent research has suggested that young people at greater risk of driving after drinking use alcohol more frequently (Vingilis et al. 1986), are more likely to demonstrate normative acceptance of DWI (Klitzner et al. 1988), and are less likely to report parental rules and restrictions regarding their travel (Williams et al. 1986).

Jonah (1986) has suggested that drinking and driving is just one component of youths' general propensity for risk-taking and has also hypothesized that risky behaviors are part of a "risk behavior syndrome" (Jonah and Dawson 1987). A review of evidence about risky driving behaviors of youths (Jonah 1986) indicated that young drivers (aged 16 to 25) are at greater risk of being involved in a crash than older drivers and that this greater risk is primarily a function of younger drivers' propensity to take risks while driving. For example, findings of studies that controlled for total distance travelled (Stewart and Sanderson 1984; Foldvary 1975) and time of day (Stewart and Sanderson 1984) indicated that younger drivers are at greater risk for crashes. Other evidence of increased risk-taking by youthful drivers includes observational field studies showing that driving speed has been found to decrease with driver age (Koneci et al. 1976). Further, young drivers receive more speeding tickets per distance travelled than older drivers (Harrington and McBride 1970), and young male drivers are involved in more rear-end collisions than older drivers (Lalonde 1979).

The possibility that individuals engaging in one risky driving behavior are likely to engage in others has also been investigated (Jonah and Dawson 1987). Research results based on self-reports of risky driving behaviors in a household survey in Canada did not support the notion of a risk behavior syndrome among drivers in general, but results did support the possibility among young drivers (aged 16 to 24) (Jonah and Dawson 1987).

The propensity for risk-taking among young DWI offenders has been investigated directly by Farrow (1987b). This assessment of decisionmaking skills and attitudes about drinking and driving compared high-school-age DWI offenders, alcohol-using juvenile offenders without DWI citations, and nonoffenders. The responses of DWI offenders indicated that they were more likely than the other groups to engage in risky driving-related behaviors. Among these risky behaviors was a greater probability of drinking before driving, associating social events and dating with alcohol use, becoming angry when questioned about driving ability, and driving fast in response to stress. The DWI offenders were also less likely to request assistance from parents than to drive while intoxicated. The author suggested that assessing youths for these risky behaviors can identify high-risk young drivers. The study's results also indicate that interventions teaching young drivers the skills required to handle or avoid risky situations may reduce drinking and driving among this population (Farrow 1987b).

To date, there is no documentation that the limited research findings about personality and behavior characteristics of those young people most likely to drink and drive have been applied to early identification and intervention efforts. For the most part, strategies that have been implemented to prevent drinking and driving among youths have targeted entire populations of young drivers, e.g., youths in high school or college. An increase in the legal minimum drinking age has proved to be a successful prevention approach and has reduced traffic crashes among young people. Driver education programs have focused on teaching young people about the risks of drinking and driving but have demonstrated very limited success in modifying youths' self-reported intentions to drink and drive. For the most part, the impact of education on actual DWI offenses or traffic safety measures has not been investigated. Environmental strategies such as designated driver programs have also been implemented but have not been systematically evaluated. (See chapter IX for a description of research on these prevention approaches.)

Factors Underlying Risky Behavior

In addition to findings indicating that people who drink and drive also engage in a variety of other dangerous driving-related behaviors (Wells-Parker et al. 1986; Donovan and Umlauf in press; Wilson and Jonah 1986, cited by Perrine 1987, 1985; Jonah and Dawson 1987; Farrow 1987b), there also is evidence that individuals who drink and drive also are more likely to engage in other health-risk and problem behaviors (Bradstock et al. 1987; Jessor 1987).

A national survey of behavioral risk factors (Bradstock et al. 1987) found that heavy smokers and individuals who did not use seat belts were more likely to drink and drive than people who did not engage in these health-risk behaviors. Individuals who drank or smoked in response to stress were more likely to drink and drive than those who exercised in response to stress; men who reported stress in interpersonal relationships were also more likely to drink and drive.

Adolescent problem behaviors such as alcohol use, smoking, use of drugs, delinquency, and precocious sexual intercourse frequently occur together in the same adolescents (Jessor and Jessor 1977; Donovan and Jessor 1985; Donovan et al. 1988). Jessor and Jessor (1977) have postulated that these behaviors may constitute a single behavioral syndrome with a single underlying cause, adolescent unconventionality in both personality and social environment. Recent research by Jessor (1987) indicated that risky driving, including driving after drinking, is part of this larger syndrome of adolescent problem behavior.

The tendency for clusters of risky behaviors to be found in certain individuals has led to the proposal that intervention must go beyond methods to prevent specific health-risk behaviors such as drinking or smoking. In this view, intervention must also include methods to determine and modify the predisposing, reinforcing, or enabling factors that underlie these risky behaviors (Ouellet et al. 1979; Rohsenow et al. 1985). It has been suggested that one reason for the failure of many programs to reduce drinking after driving among young people is that the development of such programs rarely takes into account the reasons underlying this unsafe behavior (Douglass 1982). The rationale for basing intervention programs on underlying factors is that, unless the factors are identified and addressed, they will either recur or be replaced by other risky behaviors (Bradstock et al. 1987).

Employee Assistance Programs

In the United States, nearly all alcohol-related intervention efforts in work settings are part of EAPs aimed at a range of problems including those that are alcohol related; currently, however, most workplace intervention programs specifically aimed at alcohol use problems are themselves known as EAPs. Most EAPs are based on the assumption that helping employees with alcohol use problems will reduce employee turnover and that perhaps, with intervention, employees may resume effective work performance (Roman 1988).

A national survey of worksite health promotion activities conducted in 1985 by the Office of Disease Prevention and Health Promotion (ODPHP) of the Public Health Service found that 24 percent of worksites with 50 or more workers offered EAPs (ODPHP 1987). The probability that an EAP was available was related to the size of the worksite: 52 percent of worksites with 750 or more employees had EAPs, compared to 35 percent of worksites with 250 to 749 employees, 28 percent with 100 to 249, and 15 percent with 50 to 99 (ODPHP 1987). The workplace can also be the site of programs attempting to prevent the development of alcohol use problems among employees (see chapter IX).

Types of Employee Assistance Programs

EAPs have not been standardized, but Roman (1988) has identified four types of EAPs operating in the United States: "internal" company programs, "external" company programs, labor union programs, and professional association programs. The internal company program is staffed by a company employee who accepts referrals from supervisors as well as self-referrals, conducts initial assessments, and refers employees to community resources for professional counseling or treatment. In the external company program model, which emerged during the 1970s (Roman 1988), companies contract with outside agencies to provide most services. External programs vary considerably, ranging from programs that are identical to internal programs and include a full-time program coordinator who is an employee of the outside agency, to programs that offer only a telephone number to call for assistance.

Programs in labor organizations are a third type of EAP. A descriptive study of such a program (Sonnenstuhl and Trice 1987) suggested that a peer referral process is central; a continuing process of subtle confrontation by peers is used to encourage union members with alcohol use problems to seek help.

A fourth type of assistance program, for members of professions, is usually aimed at maintaining standards of professional conduct. Threats to withdraw licensure are used to pressure members to seek assistance. This program model is most commonly applied among physicians and lawyers, but such programs also exist at the local level for dentists, pharmacists, nurses, social workers, and psychologists (Roman 1988).

At the national level, professional organizations are developing programs for their members with alcohol use problems (Trice and Sonnenstuhl 1988).

Identifying Workers Who Need Assistance

In internal and external company EAPs, the process of identifying alcohol use problems is based on job performance rather than on behavioral signs of alcohol abuse. Supervisors confront employees constructively, on the basis of poor job performance, demanding improved job performance as a condition of continued employment and offering confidential referrals for assistance. Based on the assumption that not directing attention to a person's drinking problem will reduce the probability that the person will take a defensive stance or deny the problem, this approach also restricts supervisors' involvement in the identification process to the usual supervisory activities (Roman 1988). Research by Trice and Beyer (1984) found that constructive confrontation led to improvement in employee work performance, whereas more severe forms of discipline such as written warnings or suspensions were associated with poorer performance.

Reichman et al. (1988) have suggested that an identification process based on work performance criteria yields only a small proportion of workers with alcohol use problems and that these problems tend to be more severe. They and others (R. E. Miller et al. 1988; Miller et al. 1986) have proposed that cooperative efforts between EAPs and company health-promotion programs can make it possible to identify and intervene earlier. For example, company health-promotion personnel such as fitness specialists might refer workers to an EAP; and, conversely, EAP personnel who have linked employees to interventions can also refer employees to company health-promotion activities as part of their aftercare.

Little information is available on the extent of alcohol problems in the workplace (Roman 1988) or the severity of drinking problems among individuals who become involved in EAPs. Furthermore, the management goal for such programs is to reduce absenteeism, tardiness, accidents, and other problems that affect productivity; the effectiveness of identification procedures currently used in EAPs for reaching individuals whose productivity is not reduced may not be important to employers whose primary concern is job performance (Roman 1988).

Although constructive confrontation is considered one element of a proposed core technology for company programs, self-referred workers have become a major component of these programs (Roman 1988). A variety of explanations have been suggested to account for self-referrals (Roman 1988; Trice and Sonnenstuhl 1988). One possibility is that self-referrals are a response by workers to pressures about their alcohol use problems from significant others, including supervisors (Schramm and DeFillippi 1975; Foote and Erfurt 1981; Smart 1974). Another is that self-referrals reflect the increased likelihood of Americans to seek assistance for personal problems (Roman 1988). It also has been suggested that a majority of self-referred individuals have not yet experienced a decline in job performance due to their drinking (Roman 1988). However, the self-referral process and the population of self-referred workers have not been studied systematically (Roman 1988; Trice and Sonnenstuhl 1988).

An important difference between assistance programs for professionals and other types of EAPs may be the use of clients to identify professionals requiring assistance. For example, patients may complain to local medical societies that a physician they have seen professionally may have an alcohol use problem. The degree to which client complaints may lead to identification of workers with alcohol use problems in other types of EAPs is unknown (Roman 1988).

Evaluating Employee Assistance Programs

Systematic research evaluating EAPs is very limited (Babor et al. 1986). Progress in this area has been deterred both by methodological weaknesses and by obstacles related to conducting research in an applied setting. Methodological problems have included lack of control groups, use of very brief followup periods, and reliance on subjects' self-reports (Kurtz et al. 1984). Researchers also have been hampered by difficulties in getting access to company records (Walsh 1982), as well as by poor documentation in available records and lack of access to subjects (Kurtz et al. 1984).

Roman (1988) identified a number of other areas in which research is needed. These include the social epidemiology of alcohol problems in the workplace, the relative effectiveness of the job performance criterion for identifying employee alcohol problems, assistance programs based in labor unions, the EAP self-referral process and population, and the effects of incorporating assistance for alcohol-related problems in a broader EAP model.

Intervention Programs for Children of Alcoholics

As noted earlier in this chapter, compelling evidence exists that genetics contributes to the susceptibility for alcohol dependence, but it is also clear that most offspring of alcohol-dependent parents do not become dependent themselves. To design identification and intervention approaches for those children of alcoholics who are most likely to become dependent requires isolating the psychological, social, and biological markers that specifically characterize these individuals. Although much research has been and is being conducted to identify these markers, the research base currently available does not provide enough data for developing and implementing screening programs and intervention strategies to target subgroups of the at-risk population (Blane 1988).

In addition to having a biological risk for dependence, children of alcoholics are exposed to a variety of environmental influences that may lead to alcohol use problems and other behavioral, emotional, and cognitive disorders. A number of interventions and self-help groups for children of alcoholics have emerged to address environmental influences perceived as potentially damaging. There have been efforts to increase the role of research in the design of such activities (Children of Alcoholics Foundation 1985; Russell et al. 1985), but for the most part they have developed independent of research (Blane 1988; Burk and Sher 1988).

A more extensive research base is required to document the extent to which children of alcoholics suffer behavioral, emotional, or cognitive disorders that differ in type or degree from those of other individuals who have grown up in dysfunctional families. This information will be required not only to develop suitable interventions but also to justify committing public funds and health resources (Blane 1988). Interventions also should take into account the characteristics and early experiences of members of this population who are "resilient"—that is, who function successfully—to isolate personal and environmental variables that may moderate negative influences of parental pathology (Heller et al. 1982). If such variables can be found, it may be feasible to design interventions that develop or strengthen these factors for children who are at risk.

The lack of an appropriate data base and the possibility of a negative effect from labeling individuals as children of alcoholics (Burk and Sher 1988) suggest the need for caution in targeting broad-scale intervention programs at this population. Labeling can be self-fulfilling. A classic study by Rosenthal and Jacobson (1968) demonstrated that influencing teachers' expectations about students by labeling children as intellectually "blooming" had positive effects on these students' performance (as measured by an intelligence test) that were independent of the students' actual aptitude. However, labeling also may have detrimental consequences. Although the issue of negative labeling is relevant to early identification of and intervention in alcohol use problems, little research has been conducted that directly examines this issue.

Although the deleterious effect of labeling people as "mental patients" (Temerlin 1968) and the negative connotations attached to the label "alcoholic" (Cash et al. 1984; Dean and Poremba 1983) have been demonstrated, research has not directly examined the possibility that early identification of children of alcoholics may have a negative labeling effect (Burk and Sher 1988). Few studies have examined the effects of the "at-risk" label on those who are labeled (Burk and Sher 1988). Men who were at risk for developing heart disease and who were frequently reminded of their risk status and given suggestions on coping strategies reported more efforts to change risk factors (e.g., smoking, diet) than men who were given standard medical care (Horowitz et al. 1980). However, it is not known whether these findings can be generalized to children of alcoholics (Burk and Sher 1988).

Although the data needed to develop large-scale early intervention efforts targeted at subgroups of children of alcoholics are not yet available, evidence that parental alcohol dependence is a risk factor for their offspring may serve as the basis for public information programs (Blane 1988). The need for such awareness programs is documented by the results of a recent New York State survey indicating that less than 5 percent of the general population considers children of alcoholics a group at risk (Lillis 1987). In the correct setting, interventions targeted at individuals also may be appropriate, for example, discussions with offspring of alcohol-dependent parents about their risks for future alcohol dependence, initiated by a trusted counselor or physician.

Summary

Because clinical and research interest in early and minimal intervention is relatively recent, data in these areas are limited. Few studies have been conducted, but research in the United States as well as in New Zealand, Scotland, and Sweden has suggested that relatively simple approaches to intervention can affect drinking patterns and related problems. Moderation training also holds promise for nondependent drinkers experiencing adverse consequences of alcohol (i.e., alcohol abusers), although further research is required to document the effectiveness of this approach for the target population.

Because minimal approaches to early intervention emphasize self-management techniques, there is little cost or professional involvement. Minimal interventions consist basically of combinations of brief "advice" and assessment interventions, feedback and admonition sessions, and self-help behavioral training manuals.

The need to consider the characteristics of individual DWI offenders as a means of improving the effectiveness of interventions for this population has been emphasized. Findings of recent studies suggest that interventions for drivers at greatest risk of DWI offenses should address a general propensity for risky behavior, heavy alcohol consumption, and skill at estimating BAC.

Systematic research that documents the effectiveness of treatment interventions in changing the drinking behavior of DWI offenders is presented. A California study suggests that offenders who received license actions (revocation or suspension) had fewer crashes at 4-year followup than those who were referred to treatment programs. Evidence discussed in this chapter suggests that DWI offenders may be prone to risk-taking behavior in general, and it may be this tendency that is influenced by license actions. To date, there is no documentation that the research findings about personality and behavior characteristics of youths most likely to drink and drive have been applied to early identification and intervention efforts. Most strategies have been targeted to entire populations of young drivers.

The growth of EAPs, which help workers with alcohol use problems, has continued. However, systematic research evaluating the effectiveness of such programs remains limited. The EAPs operated in companies either by company employees or by outside contractors base identification of alcohol-related problems on job performance rather than on behavioral signs of alcohol abuse. It has been pointed out, however, that this method of identification yields only a small proportion of workers with alcohol-related problems, and that these problems tend to be more severe.

The present research base does not permit the development of large-scale intervention programs for individuals who may be at risk for alcohol dependence as a result of their family history. At this time, public information programs about the risk related to parental alcohol dependence appear to be an appropriate approach to reducing risk. In the correct settings, interventions targeted at individuals and initiated by a trusted counselor or physician may also be appropriate.

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Chapter XI

Treatment

Introduction

Alcohol dependence is a serious disease that affects the health and well-being of millions of Americans. More than 1.43 million clients were treated in 5,586 alcoholism treatment units in the 12-month period ending October 30, 1987 (NIDA/NIAAA 1989). According to data from the National Drug and Alcoholism Treatment Unit Survey (NDATUS, NIDA/NIAAA 1989), 76.3 percent of clients were male; 71.5 percent were white, 15.4 percent black, and 9.9 percent Hispanic; and 55 percent were between 25 and 44 years of age. This survey also found that, as of October 30, 1987, 85 percent of clients in alcoholism treatment were receiving outpatient care; the remaining 15 percent were being treated in inpatient or residential settings, including medical detoxification settings, social detoxification units, rehabilitation/recovery programs, and custodial/domiciliary settings.

The components of treatment include management of alcohol withdrawal, long-term management of alcohol dependence, and prevention of relapse. A number of alternative treatments are available for alcohol dependence, ranging from pharmacologic therapy to counseling and marital and family therapy. Frequently two or more treatment modalities are combined in one therapeutic approach. This chapter presents a brief overview of currently used methods and approaches and describes research on newer techniques and ways of thinking about alcoholism treatment.

Management of Alcohol Dependence

Alcohol Withdrawal

Alcohol withdrawal is the first step in the management of alcoholism. Withdrawal is a highly variable and individualized phenomenon in which patients may experience none, some, or all of three major symptom types. First, autonomic nervous hyperactivity seems to account for signs and symptoms of restlessness, sweating, tachycardia, hypertension, tremors, and similar characteristics. Second, neuronal excitation may produce seizures. Third, distorted perceptions, sensations, or arousal may produce hallucinations, delirium, and disturbed sleep. Opinions vary on which medications should be used to treat alcohol withdrawal and whether detoxification should be conducted in medical or social settings.

Withdrawal Settings

The fact that a significant number of patients experience no serious medical complications during withdrawal suggests that medically oriented inpatient detoxification may be unnecessary for patients who are not severely dependent and are otherwise in good health (Diesenhaus 1982). Although the inpatient/outpatient cost ratio was 8:1, detoxification was completed by 95 percent of the inpatients but by only 72 percent of the outpatients (Hayashida et al. 1989). Holloway et al. (1984) recommended hospital care for alcoholics who lack a reliable support network and who have serious medical, neurological, or psychiatric symptoms and a history of alcohol withdrawal symptoms; others could be suitably managed in outpatient approaches. The influence of medical (pharmacologic) versus social (nonpharmacologic) withdrawal on the acceptance of and participation in continued treatment has not been established.

Protracted Withdrawal Syndrome

Several studies indicate that both acute and subacute withdrawal symptoms persist for a number of weeks. Signs and symptoms include physiological and psychological variations such as respiratory irregularity and unstable blood pressure, tension, anxiety, insomnia, and depressed mood—findings that indicate that central nervous system (CNS) hyperexcitability persists long after the removal of alcohol (Alling et al. 1982; Begleiter and Porjesz 1979; Roelofs 1985; Roelofs and Dikkenberg 1987). This constellation of symptoms has been called protracted withdrawal syndrome, subacute withdrawal syndrome, late withdrawal, and "intermediate-duration organic mental disorder associated with alcoholism" (Begleiter and Porjesz 1979; Grant et al. 1987). It appears to be the same syndrome commonly described as "dry drunks" (Flaherty et al. 1955; Hunter and Salomone 1987)—thought and behavior patterns that may precede a relapse into active alcoholism.

In a study of alcohol dependence and phobic anxiety, Stockwell, Smail, et al. (1984) suggested that panic attacks and "dry shakes" are alternative terms for the same phenomenon. This opinion is consistent with the hypothesis (Roelofs 1985) that hyperventilation and anxiety are part of the protracted withdrawal syndrome. De Soto et al. (1985) found that a high level of anxiety in the early months of abstinence decreased progressively with prolonged abstinence.

During the initial period of abstinence, such symptoms may revive a craving for alcohol and lead to renewed drinking (Kissin 1979). The physical dependency mechanisms that tend to subside with abstinence can be rapidly reactivated by drinking (Kissin 1979); in animal studies, CNS hyperexcitability is readily reactivated by exposure to ethanol, and the same effect is thought to occur in humans (Alling et al. 1982). Such findings indicate that some patients may need to be abstinent for at least 4 to 6 weeks following alcohol withdrawal to achieve the most benefit from participation in a therapeutic program (Alling et al. 1982).

Treatment Setting and Intensity

As discussed in the *Sixth Special Report to the U.S. Congress on Alcohol and Health* (USDHHS 1987), most studies evaluating treatment context have not found significant differences in outcome among inpatient, outpatient, partial hospitalization, and day clinic settings. Numerous other studies have not shown differences in outcome as a result of length of treatment.

Comparisons of this type are difficult at best because of the considerable variation in patient populations, treatment programs, and evaluation methods. Continuing research into patient-treatment matching (discussed later in this chapter) may show which treatment contexts and lengths are most appropriate for individual patients.

The Minnesota Model, as described by Cook (1988a), is an abstinence-oriented, comprehensive, multiprofessional approach to treating addictions that is based on a disease concept of drug and alcohol dependency. This intensive program promises recovery, but not cure, to those who adhere to it. The program is based on a pattern developed in Minnesota alcoholism treatment centers in the 1940s and 1950s. Treatment involves admission to a residential facility for 3 to 6 weeks and consists of lectures, group therapy, and family programs. Aftercare generally involves referral to AA. Elements of this model are discussed in detail in the next section.

Claims of good outcomes for the Minnesota Model have been supported in some studies: as many as two-thirds of the people admitted were abstinent or had reduced their drinking at 1-year followup (Cook 1988b). Studies have been criticized on methodological grounds, however, because of lack of comparability among treatment groups, attrition, short followups, and unclear outcome criteria (Cook 1988b).

Components of Treatment

Psychotherapy and Counseling

Individual and Group Therapy

Psychotherapy and counseling are traditional components of many alcoholism treatment programs. However, there is little systematic evidence about the effectiveness of counseling alone. Individual psychotherapy is seldom used alone with alcoholic patients but is usually combined with other approaches such as education about alcohol dependence, referral to AA, family intervention, and pharmacologic therapy. Group psychotherapy is a widespread and popular approach in alcoholism treatment; it is also used in conjunction with AA, pharmacologic therapy, vocational rehabilitation, and other methods.

Counseling often includes a confrontational focus, based on the rationale that alcoholics must be confronted with the reality of their problem before behavior change can take place. Hostile confrontations, however, may be associated with negative outcomes in changing behavior, especially for alcoholics with low self-esteem (Miller 1983; Annis and Chan 1983).

Brief versus extended counseling for alcoholics has been investigated. In a controlled study comparing one session of advice with extended inpatient or outpatient treatment, members of the group receiving extended treatment were found to have fewer alcohol-related problems 2 years later, although abstinence was not more common in this group (Chick et al. 1988).

Counselor behaviors and attitudes may play a critical role in the outcome of counseling; as noted in the *Sixth Special Report*, counselors differ in their abilities to keep patients in treatment, and their own personal characteristics may affect patient outcome. Research in this area is still sparse. One study found that counselors who were recovered alcoholics and older than their patients were rated more empathetic and effective by patients than those who were not recovered alcoholics (Lawson 1982); however, a study by Kirk et al. (1986) found that a counselor's history of drinking and rehabilitation did not enhance the alcoholics' perception of counselor empathy.

Group therapy has long been an essential component of alcoholism treatment programs and is often used in inpatient settings. Telch et al. (1984) found that supportive group therapy in an outpatient setting was significantly more effective in reducing reported daily drinking than group-administered covert sensitization or relaxation therapy, although no significant differences were found among the treatments on measures of blood alcohol concentration (BAC) or subjects' ratings of frequency of urges to drink. Oei and Jackson (1984) reported, in a controlled study, that using cognitive techniques in group therapy, such as reinforcing positive self-statements and relevant self-disclosures by therapists, helped maintain decreased alcohol consumption. A controlled study of self-help large-group therapy, with senior patients assuming leadership roles, found that this approach produced retention and visit rates equal to those of conventional clinic treatment based on small-group therapy (Galanter 1984). The program could be operated with half the usual counseling staff and was more effective than conventional treatment in getting inpatients to participate in subsequent outpatient care.

Individual and group psychotherapeutic approaches form the basis for the treatment model used in most alcoholism treatment programs. The goal of these rehabilitation programs is to help people with alcohol and other drug dependencies achieve abstinence and improve their lifestyles.

Family and Marital Therapy

In the past few years there has been increasing interest in family factors that maintain addictive behaviors and in the role of the family in initiating and maintaining changes in these behaviors. Family and marital problems may contribute to the original development of problem drinking, but such problems also develop as a result of the drinking and then contribute to its maintenance (McCrady 1986). Alcohol intoxication may facilitate the expression of certain family interactions while inhibiting others; these changes in relationships may serve as temporary solutions to chronic family problems and thus may stabilize the family system (Jacob and Leonard 1988). For example, Jacob and Leonard (1988) found that problem solving was more frequent among some alcoholics and their spouses during drinking episodes, a style of interaction that could have reinforcement value for the marriage that in turn reinforces continued drinking.

A number of studies have found moderately better outcomes for spouse-involved treatment for alcoholics when compared to individually focused approaches. O'Farrell et al. (1985) compared behavioral couples therapy (behavioral rehearsal and homework assignments) and interactional couples therapy (mutual support and verbal insight) for alcoholics who were also receiving traditional outpatient alcoholism treatment. In terms of improved marital satisfaction and reduced number of drinking days, couples in behavioral therapy had better outcomes immediately after treatment. McCrady and colleagues (McCrady, Noel, et al. 1986) compared three groups of alcohol-dependent individuals who received broad-spectrum behavior therapy. One group received behavioral marital therapy; the second group received couples therapy focused only on drinking; and the third group received individual therapy with minimal spouse involvement. Couples receiving the behavioral marital therapy had better outcomes in terms of drinking, marital satisfaction and stability, and well-being 18 months after treatment.

Zweben et al. (1988) studied 116 couples in which one spouse was alcoholic. The couples, who were socially stable with a moderate degree of alcohol-related difficulties and relatively nondistressed marital relationships, received either a single session of advice counseling or eight sessions of conjoint therapy. Couples in both groups showed significant improvement on all marital adjustment and drinking-related outcome measures, but there were no significant group differences in change pattern on the principal drinking outcome measure, the percentage of heavy drinking days.

Unmotivated alcoholics may reduce their drinking and initiate treatment when concerned family members are counseled in the use of appropriate procedures to reinforce reduced drinking. Sisson and Azrin (1986) conducted a study in which 12 nonalcoholic females seeking assistance because a family member was alcoholic were given either community-reinforcement counseling or a traditional type of counseling. In the community-reinforcement group, subjects received training in such areas as problem awareness, motivating change, and management of dangerous situations. The control group received traditional education, counseling, and referral to Al-Anon only. More alcoholic relatives of reinforcement group members sought formal treatment than did alcoholic relatives of the control group members. Furthermore, when they began treatment, the alcoholic relatives of reinforcement group members had already begun to reduce their drinking. Drinking was further reduced during the joint treatment of the family members and their alcoholic relatives.

Social Skills Training

Social skills training typically focuses on effective communication skills, assertiveness, and resistance to peer pressure. Oei and Jackson (1980) found that group training in social skills produced significantly faster improvement in social skills than individual training, and equivalent reduction in alcohol consumption. They also found that both group and individual social skills training produced a significantly larger reduction in alcohol consumption than traditional supportive therapy. Jones et al. (1982) studied three groups of inpatient alcoholics randomly assigned to different treatments. One group received social skills training—that is, they rehearsed their coping responses to events that might precipitate relapse. The second group only discussed the events without rehearsing their responses. The control group did neither. Outcomes in both the skills training and the discussion groups were superior to those in the control group but did not differ from each other.

In a 1-year followup study comparing the addition of social skills training to a traditional inpatient treatment program to the traditional program alone, Eriksen et al. (1986) found that those in the social skills group drank a third less than did those in the control group, which received no social skills training, and had twice as many sober days and working days. However, during drinking days the social skills group drank almost twice as much as the control group. The average length of abstinence after discharge was more than 51 days for the social skills group and slightly more than 8 days for the control group.

Alcoholics Anonymous

Alcoholics Anonymous (AA), an important component of alcoholism rehabilitation efforts, plays a central role in many therapeutic programs, providing support for both alcoholics and for their families through the Al-Anon and Alateen programs. According to the most recent AA membership survey (AA World Services 1987), there are more than 73,000 groups throughout the world. Most members are referred to AA by other AA members and by rehabilitation and counseling programs. The average member who completed the survey attends four meetings a week, and 60 percent have had prior counseling. Of the members, 66 percent are men and the predominant ages are 31 through 50. According to the survey, 29 percent have been sober more than 5 years, 38 percent have been sober 1 to 5 years, and 33 percent have been sober less than a year. The average length of sobriety among members surveyed is 52 months.

As noted in the *Sixth Special Report*, the effectiveness of AA has not been scientifically documented and methodological problems make such an evaluation difficult. In a comparison of drinking outcomes of inpatient alcoholics based on overall degree of AA attendance, however, Thurstin et al. (1987) found a higher percentage of abstinence for AA attenders, but only at 18 months after discharge. AA attenders indicated fewer drinking days during the first 6 months and fewer days drunk at 18 months. Of those subjects attending AA for the entire 18-month study period, 50 percent reported total abstinence. The investigators suggested that AA could be particularly valuable as a means of aftercare.

Other studies have found a positive association between AA attendance and abstinence (Hoffman et al. 1983; Alford 1980; Sheeren 1987), and some have suggested that AA involvement is more useful than clinical treatment in maintaining abstinence (Fry 1985; Sheeren 1987). In a review of studies of drinking outcome rates from evaluations of professional treatment that used methodology similar to that employed in studies of AA, Emrick (1987) found that AA is more often associated with maintaining total abstinence than is professional treatment; professional treatment is more often associated with alcoholics' reducing their drinking without becoming totally abstinent. However, alcohol-dependent individuals who want only to reduce their drinking probably would not join AA in the first place (Emrick 1987).

In a study of Navy enlisted men who completed treatment in alcohol rehabilitation facilities, Kolb et al. (1981) found a strong association between abstinence and AA attendance for both younger and older men. Younger men, however, were less accepting of the AA approach and apparently did not consider themselves alcohol dependent.

Boscarino (1980) reported that alcoholics who are more seriously impaired when they come to AA make less stable members. Those who are younger, male, and of lower socioeconomic status tend to have more "slips," shorter participation, and less involvement in AA activities. Ogborne and Glaser (1981) pointed out that AA is likely to be effective for that specific subgroup of alcoholics who have lost control over their drinking and believe they are powerless; these individuals are likely to find a highly structured group with clear-cut precepts such as AA effective.

Some studies have found that individuals with greater dependence on alcohol are less likely to relapse after they stop drinking (Litman et al. 1979; Edwards et al. 1987; Taylor et al. 1986). These studies showed that high dependence with AA attendance is related to abstinence and good health, and that high dependence with low AA involvement is related to high drinking levels and poor health. Edwards et al. (1987) studied factors that patients believed were important in helping them deal with their drinking and found significant differences between the 1-year followup, in which patients reported AA as less helpful, and the 10-year followup, in which AA was reported positively.

The Edwards et al. (1987) study found through factor analysis an "active" factor positively correlated with AA involvement and attendance. The active factor is similar to the finding of Maton (1988) in his study of self-help groups: Bidirectional supporters (those who both receive and provide a lot of support) reported greater well-being and group appraisal than receivers, providers, and low supporters. These findings appear to support the findings of Beckman (1980) and Giannetti (1981) that a central dimension of the AA approach is the acceptance of responsibility for one's own behavior leading to recovery, a concept similar to the active factor. These studies do not support the "enlightenment model" concept (Brickman et al. 1982; Hill 1985) in which people are blamed for causing their problems but are not believed to be responsible for solving them.

In a review of empirical studies on AA, Emrick (1987) reported that of those alcoholics who become long-term, active AA members, about 40 to 50 percent have several years of total abstinence and about 60 to 68 percent improve to some extent, drinking less or not at all during their participation. Those who combine AA with other forms of treatment seem to do as well as or better than those who only go to AA. Alford (1980) studied the effectiveness of certain AA concepts in a treatment context. The group included

56 alcoholic patients in an AA-oriented inpatient treatment setting. At 6 months, 58 percent were abstinent. However, this study addressed AA concepts as applied in a treatment setting, and not the fellowship of AA.

Pharmacologic Treatment

In the past decade, research into the pharmacologic treatment of alcoholism has become increasingly active, and a majority of physicians in private practice are reported to prescribe pharmacologic agents for the treatment of alcoholism (Sellers et al. 1981). Four types of pharmacologic agents have been used in treatment for alcohol dependence: agents that manage withdrawal; agents that foster sobriety in dependent individuals; agents that decrease drinking by treating associated psychiatric pathology; and agents that attenuate problem drinking behavior itself. Pharmacologic agents alone, however, are unlikely to be effective in producing long-lasting reduction in drinking behavior, and they should be considered adjuncts to existing treatment strategies.

Agents That Manage Withdrawal

For more than two decades the benzodiazepines (such as Librium and Valium, among others) have been considered the best medications for alcohol withdrawal. These agents are effective in managing the major and minor features of the withdrawal syndrome, including seizures and hypertension, and in preventing delirium tremens. Before the introduction of benzodiazepines, delirium tremens was relatively common during withdrawal, but now this life-threatening condition is rare. Both the long-acting benzodiazepines, chlordiazepoxide (Librium) and diazepam (Valium), and the shorter-acting benzodiazepines, oxazepam (Serax) and lorazepam (Ativan), are considered the drugs of choice (Liskow and Goodwin 1987).

Physicians traditionally have used benzodiazepines by administering decreasing doses over the period of alcohol withdrawal. Rosenbloom (1988) recommends this approach, suggesting the use of intermediate half-life benzodiazepines (such as lorazepam), or even shorter half-life drugs (such as midazolam). These drugs do not linger in the system and thus allow doses to be easily titrated to the patient's response. Sellers et al. (1983), however, introduced a different approach that involves loading doses of diazepam, which itself has a long-life and produces a psychoactive metabolite (desmethyldiazepam) with an even longer half-life. Loading doses are administered as needed every 1 to 2 hours only at the beginning of treatment. This strategy simplifies treatment and eliminates possible reinforcement of drug-seeking behavior in patients who otherwise might receive additional medication for relief of symptoms.

Other agents with known effects on adrenergic systems have been used in the treatment of alcohol withdrawal. Clonidine, a centrally active alpha-2-adrenergic agonist used in the treatment of hypertension, has been reported to reduce some symptoms of withdrawal in randomized double-blind controlled studies (Liskow and Goodwin 1987). Part of the interest in clonidine treatment of alcohol withdrawal arises from its demonstrated success in the treatment of opioid withdrawal and from the similarity of some neurochemical changes in opioid and alcohol abstinence. Tremor and the cardiovascular symptoms of tachycardia and hypertension have been found to be alleviated by clonidine; however, there is much less agreement about its effects on other symptoms.

Past research (Sellers et al. 1977) in which the beta adrenergic blocker propranolol was administered alone suggested some benefit from such compounds. More recently another beta blocker, atenolol, was found to attenuate alcohol withdrawal symptoms and lead to faster recovery when given in combination with the benzodiazepine oxazepam (Kraus et al. 1985). Beta blockers may be effective because they counteract hyperadrenergic withdrawal symptoms such as tachycardia and hypertension. Both the beta and alpha adrenergic agents, however, have little apparent value in treating the very serious symptoms of seizures and delirium frequently seen with alcohol withdrawal. Therefore, treatment should include a combination of these agents with an effective anticonvulsant.

Several other agents with potential value in the treatment of withdrawal are in the early stages of evaluation. These include calcium channel blockers (Koppi et al. 1987), anticonvulsants such as carbamazepine and valproate (Linnoila et al. 1987; Roy-Byrne 1988), and non-benzodiazepine sedative hypnotics such as chlormethiazole (Robinson et al. 1989).

Agents That Foster Sobriety

Disulfiram (Antabuse) has been widely used since the 1950s as an aversive medication to treat alcohol dependence. Disulfiram inhibits the enzyme aldehyde dehydrogenase (ALDH), one of the major alcohol-metabolizing enzymes, causing increases in blood acetaldehyde levels after alcohol is consumed. This results in a toxic physiological response which tends to foster sobriety. Many of the complexities surrounding the therapeutic use of disulfiram were addressed in the *Sixth Special Report*. A well-designed, controlled, randomized study (Fuller et al. 1986) found that disulfiram reduced the frequency of drinking in a substantial proportion of men who did not remain abstinent but that it did not contribute to sustained abstinence, relapse delay, or other indicators of social stability any more than counseling alone. In this study, however, use of disulfiram was unsupervised. Sereny et al. (1986) reported that significant periods of sobriety up to 12 months were achieved in 60 percent of patients who participated in a supervised disulfiram therapy program in a clinic three times a week as a condition of their remaining connected to the clinic. The investigators concluded that this supervised approach warrants more extensive investigation.

As with any other pharmacologic approach, the efficacy of disulfiram may be reduced by poor compliance. Kofoed (1987) found that disulfiram compliance could be increased by the clinical use of chemical monitoring data obtained through a breathalyzer technique. In this study, however, increased disulfiram compliance did not correlate with other aspects of treatment compliance or effectiveness as measured by duration of outpatient treatment and scores in the drinking behavior interview.

Calcium carbimide (Temposil, Abstem) has received increasing attention for use as an ethanol-sensitizing agent, although it is not available in the United States. It inhibits ALDH for approximately 24 hours and could theoretically be used as needed by alcoholics in situations where they would be likely to drink (Peachey and Annis 1985). Unlike disulfiram, calcium carbimide does not block dopamine beta hydroxylase, a key enzyme in the production of adrenaline and noradrenaline, and has fewer adverse side effects (Peachey and Annis 1984). As with disulfiram, however, concern has been raised about its possible toxic effects on the liver after prolonged use (Vazquez et al. 1983). In a randomized, double-blind, placebo-controlled study of calcium carbimide (Peachey et al. 1989) all of 69 analyzable subjects who completed the study were abstinent at least 85 percent of the time, and 40 were alcohol free during the study. Symptoms and adverse reactions with calcium carbimide were not greater than those reported with the placebo. A significant proportion of the patients believed they were receiving calcium carbimide during the study, suggesting that calcium carbimide exerts a strong psychological deterrent effect. However, there was no evidence of a pharmacologic effect of calcium carbimide on drinking behavior; compared to pretreatment levels, alcohol consumption was significantly reduced equally with both calcium carbimide and placebo (Peachey et al. 1989).

Nitrefazole, now being tested in Europe, is similar to disulfiram in inhibiting ALDH for long periods and is effective within an hour of administration (Liskow and Goodwin 1987).

In summary, disulfiram may be of value in helping some alcoholics abstain, probably because alcoholics fear its aversive consequences; research suggests that it may be more effective if given in a supervised setting. Calcium carbimide may be an effective aversive agent, although controlled studies are needed to assess its value and safety. Nitrefazole may be of value as an aversive drug for up to 3 days after a single dose (Stockwell, Sutherland, and Edwards 1984) but has yet to be evaluated extensively.

Agents That Attenuate Drinking Behavior

The discovery and evaluation of pharmacologic agents that may reduce alcohol craving and drinking depend on the ability of research to provide a better understanding of the complex neurobehavioral and neurobiological factors that regulate alcohol intake. Several neurotransmitters and neurohormones have been implicated in the acquisition, maintenance, and cessation of alcohol consumption. Continued research on the mechanisms underlying these behaviors may yield more clinically useful pharmacologic treatments.

A number of compounds with specific effects on brain neurotransmitters have been found to reduce alcohol consumption in experimental animals. The opioid antagonists naloxone and naltrexone have been shown to reduce alcohol consumption in rodents and primates (see chapter IV). Naloxone has also been reported to reduce alcohol-induced respiratory depression, but clinical evaluation of opioid antagonists for alcohol dependency has not occurred. There has been some interesting research on the possible use of pharmacologic agents that are specific to dopamine in reducing drinking. Dopamine has been implicated in several behavioral effects of alcohol, particularly its reinforcing effects (see chapter IV). Bromocriptine, a dopamine agonist, has been reported to be superior to placebos in reducing drinking and craving for alcohol in severely dependent individuals (Borg 1983).

Recently, very promising basic neuroscience research has generated considerable interest in GABA-benzodiazepine systems (see chapter IV) and the treatment potential of compounds specific to these systems. Ro15-4513, an experimental agent that specifically interacts with GABA-benzodiazepine receptors in the brain has been shown to reduce alcohol intoxication and anxiolytic effects of alcohol (Suzdak et al. 1986) as well as alcohol consumption in experimental animals (McBride et al. 1988). Because of known intrinsic properties and unknown toxicity, this compound has not been considered for possible use in the treatment of alcohol dependency.

The most promising group of pharmacological agents in reducing alcohol consumption is the serotonin uptake inhibitors. These agents reduce re-uptake of the serotonin by neurons and thereby increase the activity of this important neurotransmitter. Several of these compounds have been shown to reduce alcohol consumption in experimental animals (see Naranjo, Sellers, and Lawrin 1986 for review) and more recently have been evaluated clinically. Fluvoxamine, fluoxetine, and citalopram have been found to reduce alcohol consumption in nondependent problem drinkers (Naranjo, Sellers, and Lawrin 1986). These compounds have been considered promising because unlike some serotonin uptake inhibitors (e.g., zimelidine) they seem relatively safe with few side effects.

Another promising agent in reducing alcohol consumption is buspirone, a relatively new nonbenzodiazepine anxiolytic. It has been shown to reduce alcohol consumption in monkeys (Collins and Myers 1987). Preliminary clinical studies suggest that this compound may modify craving, particularly in alcohol-dependent individuals who also have high levels of anxiety. This agent has several advantages over benzodiazepine anxiolytics in having minimal interaction with alcohol, very low abuse potential, and no risk of physical dependence. As with the previous group of agents, it is believed that the therapeutic action of buspirone is due in part to its ability to block serotonin uptake.

Considerable further basic and clinical research is needed on all of these pharmacologic agents to determine the mechanisms that are the basis of their therapeutic effect, the clinical populations for which they may be appropriate, and the possible complications that render them inappropriate. The role that they will play in the treatment of alcohol dependency will of course rest on these findings; however, they offer the prospect of a valuable component to supplemental nonpharmacologic treatment of the disease.

Aversion Therapy

Aversion therapy is based on conditioning theory that postulates that the sight, smell, and taste of alcohol will acquire aversive properties if repeatedly paired with noxious stimuli. Nathan (1985) pointed out that the success rates in chemical aversion therapy programs can be attributed to the likelihood that the alcoholics undergoing this therapy enter treatment with better prognoses than those who enter other kinds of treatment. They are a largely homogeneous group of well-motivated, well-educated, relatively stable people with the financial resources for the program. Furthermore, because these treatment programs often involve nonaversive forms of treatment as well, and because many studies of treatment effects have been uncontrolled, the contribution of chemical aversion alone cannot be rigidly evaluated (Nathan 1985; Wilson 1987). Other considerations in chemical aversion therapy include safety, intrusiveness, acceptability, availability of alternative methods, and economy (Wilson 1987).

A type of aversion therapy called covert sensitization involves the use of verbal suggestion to associate imagined drinking with unpleasant experiences such as nausea. In one study of this technique (Elkins 1980), imaginary drinking scenes emphasizing motivational, sensory, and behavioral concomitants of alcohol ingestion were paired with nausea induced by verbal suggestion in 57 subjects. Of these, 24 developed some degree of conditioned nausea. Mean total abstinence after discharge for these 24 conditioned subjects was more than 13 months, significantly longer than for others in the study. When their drinking status was assessed, the conditioned subjects were mostly in the abstinent and normal-drinking categories, whereas nonconditioned subjects were generally excessive drinkers.

Miller and Dougher (in press) assigned 29 outpatients with a history of problem drinking and alcohol dependence to one of three covert sensitization conditions in which the stimuli in aversion scenes were varied. Group 1 were exposed to scenes of nausea and vomiting induced by drinking; group 2, to similar scenes assisted by noxious odors; and group 3, to scenes of disturbing potential consequences of drinking ("anxiety conditioning"). At 18 months' followup, abstinent, controlled, or improved outcomes were observed in 45, 56, and 67 percent of the subjects in the three groups respectively, although the treatments did not differ significantly in effectiveness. Current research is inadequate to evaluate the potential role of covert sensitization in alcoholism therapy because most studies have not been conducted under controlled conditions. However, covert sensitization may eventually be a useful addition to broader treatment strategies.

Relapse Prevention

Relapse prevention is a behavioral approach that has received increasing research attention. This approach emphasizes the importance of environmental cues in relapse and helps people develop a set of coping strategies to deal with situations that present a high risk for drinking. Relapse prevention focuses on maintaining changes in drinking behavior over time in a natural environment. Critical to this approach is the alcoholic's developing a strong sense of personal confidence or self-efficacy in coping with drinking situations. Further, in the event that the alcoholic should take a drink, this behavior itself would not necessarily lead to a full-blown relapse (Annis and Davis 1988).

A model of relapse proposed by Marlatt (1985) suggests that any drinking episode can be analyzed according to five major variables: (1) exposure to situations that hold high risk for drinking; (2) use or nonuse of successful coping responses in these situations; (3) enhanced self-efficacy for coping or reduced self-efficacy for noncoping; (4) expectancies about the effects of alcohol in the situation; and (5) the abstinence violation effect—the alcoholic's cognitive and emotional reaction to the ingesting of alcohol.

As part of an inpatient treatment program, Chaney et al. (1978) studied how training in coping skills affected relapse. They found that the relapse prevention group (those patients who received the coping skills training) had a longer period of abstinence than others, but they found no differences in absolute abstinence or percentage of subjects that did not relapse at all. There were significant differences in favor of the relapse prevention group for decreased duration and severity of drinking, however.

Litman (1986) and Litman et al. (1984) demonstrated a direct relationship between the alcoholic's perception of self-efficacy in coping behaviors and subsequent outcome. Alcoholics who relapsed 6 to 15 months after hospital treatment perceived more situations as risk factors for relapse and felt that they had less control over their own unpleasant emotional states and were more vulnerable to external events. They did not believe their coping behaviors were effective and did not see relationships between the situations they perceived to be dangerous and their own ability to deal with them. Those who did not relapse during this period perceived both positive thinking and avoidance as effective coping behaviors and perceived fewer situations as dangerous to their continued abstinence. As they continued to abstain, they tended to use avoidance less and positive thinking more. The more they experienced their coping behaviors as effective, the less they perceived situations as dangerous.

In an alcoholism treatment program, Annis and Davis (1988) implemented a trial of relapse prevention that emphasized coping techniques in 41 clients who were followed up at 3 and 6 months after being discharged from treatment. In addition to marked decreases in alcohol consumption and substantially improved ratings of self-efficacy, most clients reported improvement in a wide range of areas of personal and social functioning. From a mean of 46 drinks a week at intake, the average reported consumption had decreased to fewer than two drinks a week at 3 months and to fewer than six drinks a week at 6 months. After 3 months, 47 percent reported total abstinence, and after 6 months, 29 percent.

A related approach, cue exposure with response prevention, is based on research showing that alcoholics with the greatest degrees of alcohol dependence also show the strongest conditioning to alcohol cues. Drinking occurs in response to physical cues commonly associated with drinking, to negative and positive emotional states, and to small doses of alcohol (Niaura et al. 1988; Rankin 1986). These observations have led to a treatment in which alcoholics are repeatedly exposed to both alcohol and alcohol-associated cues but are prevented from drinking in response. After a series of exposures and preventions, the conditioned response to alcohol is expected to be extinguished, with the result that one drink may no longer lead to impaired control. Using this approach with a small "priming" dose of alcohol, Rankin et al. (1983) demonstrated a significant decrease in craving. Although this approach appears promising, its relationship to treatment outcome has not yet been demonstrated.

Psychiatric Disorders Among Alcoholics in Treatment

The presence of psychiatric disorders in alcoholics may have important implications for therapeutic approaches and clinical management as well as eventual outcome. Furthermore, neuropsychological impairments that have been found in chronic alcoholics suggest that alcoholics' cognitive deficits may render some types of therapeutic formats less effective, especially early in the treatment process.

A survey evaluating the lifetime and current prevalence of mental disorders in patients seeking assistance for alcohol and other drug problems found that 78 percent had a history of psychiatric disorder in addition to substance abuse and 65 percent had a current mental disorder (Ross et al. 1988). In this study, patients who abused both alcohol and other drugs were the most psychiatrically impaired. In a population study of 20,000 people, psychiatric diagnoses were more likely to occur in alcoholics than in nonalcoholics, and associations were particularly strong for alcoholism and antisocial personality disorder, other substance abuse, and mania (Helzer and Pryzbeck 1988).

Persistent heavy drinking also may be associated with symptoms of anxiety, depression, confusion, or psychosis (Schuckit 1986). Transient psychiatric symptoms may be less common forms of withdrawal symptoms and must not be confused with other disorders (Blankfield 1986). Thus it is important to discriminate between symptoms and syndromes to determine if the psychopathology is part of a non-alcohol-related psychiatric disorder or if it is part of a transient state of alcohol withdrawal.

As noted in the *Sixth Special Report*, several studies have shown that patients with severe psychiatric problems do poorly regardless of the type of treatment they receive, whereas those with less severe psychiatric problems may improve in many types of treatment programs. Rounsaville et al. (1987) recently studied psychopathology as a predictor of treatment outcome in 266 alcoholics, again finding that coexistent psychiatric diagnoses such as major depression or antisocial personality generally predicted poorer outcome among males. Among women, however, having a major depression was associated with a better outcome in drinking-related measures, whereas antisocial personality and drug abuse were associated with a poorer prognosis, suggesting that the posttreatment course in male and female alcoholics may be influenced by different factors.

Alcoholism and major depression appear to be independent entities, but symptoms of depression may develop during the course of alcoholism, and some patients with affective disorders may drink more when they are ill (Schuckit 1986). Substance abuse also may increase the intensity of symptoms of preexisting primary psychiatric disorders (Schuckit and Monteiro 1988). However, research studies indicate that 70 to 80 percent of patients with severe depression do not increase their drinking, and that only 5 to 10 percent of patients with primary major depressive disorders actually develop secondary alcoholism (Schuckit and Monteiro 1988).

Although some of the same symptoms may be present in both alcoholism and major depression, variations in the course and treatment of the two disorders make it important to differentiate between primary depression and transient depressive symptoms in alcoholism (Dorus et al. 1987). In a study of male primary alcoholics with no preexisting depressive disorders, Brown and Schuckit (1988) found that during the first week of abstinence more than 40 percent had depressive symptoms comparable to those seen in patients hospitalized for primary depression. For the majority, however, depressive symptoms remitted by the second week of treatment and continued to decrease during 3 to 4 weeks of abstinence. After 3 weeks of abstinence, depression is uncommon. If it does persist, however, specific interventions may be required (Brown and Schuckit 1988).

Dorus et al. (1987) examined depressive symptoms in 50 inpatient alcoholics and found major depression in 16 of them (32 percent). Depressive symptoms decreased markedly as patients progressed from active drinking to abstinence; the highest level of depression occurred during active drinking before onset of any significant withdrawal symptoms. Symptoms of depression decreased during withdrawal and were least severe during abstinence. By day 10 of abstinence, the unstable mood and cognitive

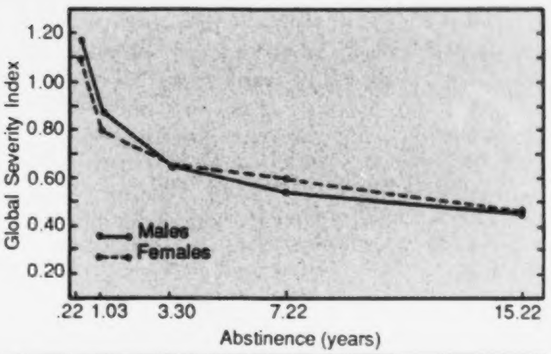

FIGURE 1. Severity of symptoms (mean scores on the Global Severity Index of the SCL-90-R) for subjects grouped by sex and length of abstinence.
SOURCE: De Soto et al. 1985. Copyright 1985 by the Research Society on Alcoholism.

impairment characteristic of active drinking had resolved.

Many studies have reported high levels of anxiety among alcoholics, especially during the first several weeks of abstinence, but additional data indicate that these symptoms are likely to decrease with continued abstinence and are not an independent anxiety disorder (Schuckit and Monteiro 1988). De Soto et al. (1985), in a cross-sectional study, found that symptomatology among alcoholics of both sexes was high in the initial 6 months of abstinence, with levels of distress diminishing over time (see fig. 1). Distress was greatest on three symptom dimensions: depression, obsessive-compulsive, and interpersonal sensitivity. A followup study of the same subjects (De Soto et al. 1989) also found symptomatology among abstinent alcoholics to decrease over time, suggesting a recovery process.

In a recent study of anxiety symptoms among 171 primary alcoholic men, Schuckit et al. (in press) found that almost all reported at least one symptom of anxiety during drinking or withdrawal, including palpitations or shortness of breath. A few experienced panic attacks during heavy drinking or withdrawal, although no such attacks occurred before the onset of heavy drinking or during protracted abstinence. The investigators concluded that there did not appear to be an elevated incidence of either panic disorder or generalized anxiety independent of heavy drinking.

Most alcoholics entering treatment do not have decreased overall intelligence scores, but upon neuropsychological testing approximately 45 to 70 percent of these patients have specific deficits in problem solving, abstract thinking, concept shifting, psychomotor performance, and difficult memory tasks (Parsons and Leber 1981; Eckhardt and Martin 1986; Tabakoff and Petersen 1988). Pronounced neuropsychological impairment is also often evident in alcoholics who have stopped drinking, although it generally becomes less pronounced as the length of abstinence increases (Goldman 1986). Several studies have indicated that alcoholics have impaired ability to learn the informational content presented in a treatment program for up to a month after they have stopped drinking (Goldman 1986; Becker and Jaffe 1984; McCrady and Smith 1986). Cognitive impairments should therefore be taken into account in treatment programs for alcoholics, and such treatment programs may need to be modified to enhance cognitive recovery (Goldman 1987). For further discussion of this topic, see the *Sixth Special Report*.

Pharmacologic Treatment of Associated Psychiatric Illnesses

The high coincidence of alcohol dependency and depression has led to considerable interest in the potential value of pharmacologic treatments for affective disorders in the treatment of alcoholism. There was much enthusiasm for the possibility that lithium salts might prove effective in reducing alcohol abuse. Research on the effectiveness of lithium, however, has not shown significant reductions in alcohol consumption (Peck et al. 1981; Powell et al. 1986). Fawcett et al. (1984) found higher rates of abstinence at 18 months in patients taking lithium than in a placebo treatment group, but both groups also had a high rate of major depression. In subsequent work, Fawcett et al. (1987) concluded that lithium may affect drinking behavior in a way that is unrelated to the treatment of affective symptoms. In this study, serum lithium levels and abstinence rates were not linearly associated, but subjects who started lithium therapy as inpatients were significantly less likely to relapse during the first month than were patients who complied with placebo treatment. There was no evidence that depressed alcoholics responded better to treatment than nondepressed alcoholics or that lithium had any significant impact on the mood or social adjustment of alcoholics.

In a multisite clinical trial, Dorus et al. (1989) assessed the efficacy of lithium in the treatment of 457 male alcoholics in a double-blind, placebo-controlled study. Alcoholics with and without a history of major depression were studied. The investigators found no significant differences between those taking lithium and those taking a placebo on the following outcome measures: number of alcoholic patients abstinent, number of days of drinking, number of alcohol-related hospitalizations, change in rating of alcoholism severity, and change in severity of depression. The investigators concluded that lithium does not affect the course of alcoholism in either depressed or nondepressed alcoholics.

Patient-Treatment Matching

Differences in responses to treatment based on variations in patient and treatment characteristics have led to an interest in patient-treatment matching. According to this approach, selectively matching client populations with facilities, treatment methods, and treatment providers may significantly enhance treatment effectiveness and improve treatment outcomes (Pattison 1985). Researchers have been exploring the advantages of alternative treatment strategies for patients with different psychological and behavioral characteristics. For example, with the development of procedures to measure the severity of alcohol dependence, it may be possible to assign patients to different types and intensities of treatment based on their severity of dependence and suitability for different therapies. Other issues in this area include matching patients to treatments according to such characteristics as age, sex, ethnic group, and family history of alcoholism.

Indicators of various levels of intellectual functioning and of social stability or social competence appear to be associated with treatment outcome in certain treatments (Gibbs 1981). At present there is some evidence to suggest that psychopathology is associated with a poorer prognosis, indicating that these types of patients may warrant more individualized or intensive attention (McLellan et al. 1983). A classification system based on measures of intellectual functioning and social stability may help to explain factors that appear to have been confused with outcome in previous evaluation studies; instead of asking which treatment works best for alcoholics, the more appropriate question may be which treatment works best for what type of alcoholic (Gibbs 1981).

Miller (1989) has proposed a self-matching approach in which the individual is presented with an array of options, given an accurate description of each, and encouraged to choose the approach that seems most appropriate. The self-chosen option may be more likely to be followed, thereby improving chances for recovery (Miller 1985).

Several studies have suggested that varying degrees of emotional or life adjustment problems require different intensities of treatment (McLellan et al. 1983). Alcoholic patients with both severe alcohol dependence and life adjustment problems did better in a structured, full hospital treatment program than in a partial hospitalization program (McLellan et al. 1983). Annis and Chan (1983) found that alcoholic patients who are high in self-esteem seem to do better with therapies that use confrontational approaches than do those who are low in self-esteem. Other work indicates that patients who think in abstract, analytical ways do better with therapists who also think in these ways (McLachlan 1974).

Although important findings about patient-treatment matching from individual studies have been reported, the utility of these findings to the alcoholism treatment field is limited because of questions about generalizability. Because individual studies have rarely offered the opportunity to test standardized treatment regimens in multiple samples, it is difficult to determine whether conclusions about patient-treatment matching can be generalized from the specific population studied to other populations and to different settings. Research in this area has also been impeded by samples that are generally too small to permit precise measurement of the effect of patient-treatment matching on treatment outcome. Multisite trials will be helpful in resolving some of these issues.

The optimal relationship between the type of treatment and the type of patient is just beginning to be explored; furthermore, matching effects may make a substantial contribution to explaining variations in treatment outcome (Annis 1988). Patient-treatment matching is discussed more fully in the *Sixth Special Report*.

Outcome Evaluation Methods

Interest in research into outcome evaluation has been increasing in the alcoholism treatment field. The dominant approach has been to investigate the effectiveness of a treatment by means of traditional evaluation methods that examine the main effects of different treatments compared to no treatment or alternative treatments. A comprehensive review of evaluation methods (Sobell et al. 1987) noted that because no single source of outcome data is free from error, the trend is to use multiple sources of outcome data and seek corroboration. Although self-reports have been the most frequently used data source, collateral reports are being used with increasing frequency. The quantity and frequency of drinking as a measure for outcome has also been called into question, because this measure may sometimes fail to identify clinically important but atypical episodes of heavy drinking (Sobell et al. 1987). For more information on screening instruments and procedures, see chapter VIII.

Advances in evaluation methodologies have contributed to more accurate estimation of the relative contributions of therapeutic interventions, program settings, environmental variables, and patient characteristics in the success or failure of treatment. Evaluations have traditionally been difficult because of the complexity of the treatment system. Alcoholics are often exposed to several different treatment providers and therapeutic approaches in the same setting and then move through a series of settings during the course of treatment and recovery. Such a mixture may overwhelm the individual contributions of specific treatment variables or components.

Furthermore, traditional evaluation methods may be too global and imprecise because the therapeutic change is multidimensional. The growing consensus is that treatment outcome should be evaluated according to multiple variables such as alcohol and other drug use, vocational adjustment, psychological problem severity, interpersonal relations, and criminal behavior (Emrick and Hansen 1983; McLellan et al. 1983). Taylor et al. (1986) argued for analyzing the many variables in relation to one another rather than individually.

In a correlational and factor analysis study, Babor et al. (1988) reported that posttreatment drinking is related to poor outcome in both social and psychological functioning and that the level of posttreatment alcohol consumption is directly related to changes in medical status, life stresses, and psychopathology. They cautioned that before a unidimensional measure of outcome is abandoned, attention should be directed toward the role of posttreatment alcohol consumption in mediating posttreatment status across a wide variety of dimensions. They suggested that evaluation of treatment should focus on at least three levels of analysis: (1) specific indicators of drinking behavior, (2) various areas of life functioning and health, and (3) a global dimension of outcome that encompasses drinking behavior and its consequences and the type of treatment used.

Another important trend in specifying outcome variables has been the growing attention to "process" measures (Moos and Finney 1983). Process analysis focuses attention on the causal link between specific treatment components and dimensions of outcome.

Self-report procedures, such as interviews, tests, and questionnaires, have become the major method of obtaining clinical data on alcohol abuse and treatment. However, questions have been raised about reliance on self-reports in outcome studies. In one investigation of the validity of self-reports, Watson et al. (1984) found that barely half the variance in the alcoholics' self-reports corresponded to assessments of the alcoholics' drinking behavior made by collaterals (cohabiting friends or relatives). Comparison of collateral reports with alcoholics' self-reports suggested that alcoholics may have underestimated their alcohol use about three times as often as they overestimated it.

Fuller et al. (1988) analyzed the validity of self-reports in a major longitudinal Veterans Administration cooperative study evaluating the efficacy of disulfiram treatment and concluded that self-reports are not a valid method of measuring treatment response. In this study, self-reports, collateral interviews, and blood and urine alcohol tests were used to evaluate drinking behavior. The self-reported rate of relapse was nearly 59 percent; however, a combination of assessment indicators revealed a rate of slightly more than 72 percent. Patient-collateral pairs agreed on number of drinking days less than half the time, and collaterals were three times more likely to report more drinking days than the patients were. The investigators reported only 65-percent probability that patients who claimed continuous abstinence for a year were in fact continuously abstinent.

In a review of the usefulness of self-reports and biological measures of alcohol consumption in outcome studies, O'Farrell and Maisto (1987) found that research showed adequate internal consistency and test-retest reliability for a variety of self-report measures of drinking behavior. For reports of amount consumed, reliability was good for outpatient alcoholics but was less adequate for those seen in inpatient and residential settings who may be more chronic, less socially stable, and more severely alcoholic. However, alcoholics whose positive BAC showed they had been drinking before the interview were more likely to give invalid self-reports than those with a zero BAC. O'Farrell and Maisto noted that alcoholics' cognitive impairment and collaterals' lack of contact with and detailed knowledge of certain aspects of the alcoholics' behavior may contribute to discrepancies between self-reports and collateral reports.

Tracking chemical markers of alcohol consumption (see chapter VIII) has been proposed as a method for assessing treatment outcome. O'Farrell and Maisto (1987) noted that markers correlate only modestly with self-reported consumption, are affected by other factors, and show large individual differences in response to alcohol intake—in short, available biological markers do not provide a "gold standard" for alcohol consumption. Nevertheless, O'Farrell and Maisto suggested that markers can be used as a verification measure and as a measure of negative alcohol-related health consequences. Irwin et al. (1988) reported that serial changes in three test values—gamma-glutamyltransferase, aspartate aminotransferase, and alanine aminotransferase—can be used to distinguish abstinent alcoholics from those who have returned to drinking, a promising approach to resolving problems posed by tracking biological markers.

Babor et al. (1987) noted that such studies raise fundamental questions about the accuracy of data derived from verbal report procedures, especially when used to evaluate the effectiveness of treatment outcome. Their review of methodological studies in the alcohol literature shows that although the information obtained from alcoholics and heavy drinkers tends to be reliable and valid, several factors can lead to variability in accuracy, such as the sensitivity of the information sought, the specificity of the validation criteria, and the personal characteristics of the respondents. Babor et al. (1987) also reviewed several methodological techniques likely to enhance the validity of self-reports. Treatment outcome research cannot be done without using self-reports; self-reports may be supplemented best by other measures such as collateral reports or biomedical verification techniques.

Summary

During fiscal year 1987 more than 1.43 million people were treated for alcoholism, the majority in outpatient settings. Withdrawal, the first step in treatment, is a highly variable phenomenon: some alcoholics may need hospital care for this phase of treatment, whereas others may do equally well in other settings. For some alcoholics psychologically supportive care will be sufficient, but medication therapy is typically employed for those with moderate to severe withdrawal signs and symptoms.

No pharmacologic intervention by itself appears to decrease alcohol consumption for a long period, and medications are usually combined with other forms of treatment in alcoholism therapy. Disulfiram (Antabuse) continues to be widely used, and recent research focuses on ways to increase patient compliance with the therapeutic regimen. Pharmacologic agents that affect neurotransmitters related to alcohol dependence may offer some promise for improved pharmacotherapy. A type of aversion therapy—covert sensitization—is currently being investigated and may prove to be a useful adjunct to broader treatment approaches.

Counseling, psychotherapy, and AA are traditional therapeutic approaches that still form the foundation in many treatment programs. Methodological problems make rigorous, controlled evaluations of these approaches difficult, although they appear helpful for a substantial number of alcoholics.

An emerging picture in alcoholism treatment is that of a broad-based process, with interventions directed both at changing drinking behavior itself and at changing the alcoholic's environment and other life problems in ways that will help maintain sobriety. Approaches such as social skills training, family and marital therapy, and relapse prevention techniques focus on both drinking behavior and life circumstances.

Advances in outcome evaluation methods have made it possible to evaluate treatment outcomes more accurately. Questions have been raised about the validity of alcoholics' self-reports about drinking behavior in outcome studies, and there is a trend to obtain collateral and biochemical verification of such reports. Outcome evaluation is being directed with increasing frequency toward evaluation on several dimensions, not just drinking behavior. Because alcoholics often receive a variety of treatments during alcoholism therapy, it is difficult to compare the absolute effectiveness of one treatment with another. Continued research into patient-treatment matching may eventually make it possible to assign patients to treatments that are more likely to succeed in light of individual patient characteristics.

Psychiatric disorders are prevalent among alcoholics. Regardless of the treatment they receive, alcoholic patients with psychiatric problems seem to do less well than alcoholic patients without these problems. However, depression and alcoholism appear to be independent entities, and in treating alcoholics it is important to distinguish transient depressive symptoms from major depression. Neuropsychological impairment may be evident in alcoholics who have stopped drinking and needs to be taken into account in treatment programs.

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